Versatile Therapeutic effects of Vinca rosea Linn.: 

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Abstract:

The Plants Kingdom still remains to be the primary source of Medicine. It has been proved to be efficient enough to treat many diseases including the world’s most Dreadful disease tumor with nil or minimum side effects. Considerable studies have been carried out on ethnomedicinal plants of India; however, only few medicinal plants have attracted the interest of scientists. Concomitant with the preparation of clinically useful compounds from ancient plant remedies there has been an increased interest in studying the pharmacological action of the plant alkaloids. Vinca rosea has been the thought of interest for most of the Pharmaceutical scientists for more than two decades. Vinca rosea is of importance due to its anti tumor and anti diabetic actions.

Aim of the Review:

The purpose of this review is to bring into light the versatile remedial effects of Vinca rosea against tumor and Diabetes along with its other biological activities.

Introduction:

The plant Vinca rosea Linn (periwinkle) is an apocynaceous, ever-blooming, pubescent herb or sub-shrub which has been shown to be a source of many alkaloids. It has enjoyed a popular reputation in indigenous medicine in various parts of the world.[1]

Fig.1-Vinca rosea
Table 1: Systematic classification of *Vinca rosea*  

<table>
<thead>
<tr>
<th>Botanical Name :</th>
<th><em>Vinca rosea</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientific name:</td>
<td><em>Catharanthus roseus</em></td>
</tr>
<tr>
<td>Family Name</td>
<td>Apocynaceae</td>
</tr>
<tr>
<td>Common Name</td>
<td><em>Periwinkle, Madagascar Periwinkle, Sadabahar</em></td>
</tr>
<tr>
<td>Part Used</td>
<td>Seed, Root, Whole plant, Leave</td>
</tr>
<tr>
<td>Habitat</td>
<td>Grows throughout India and found as an escape in waste places sandy tracts</td>
</tr>
</tbody>
</table>

**General Uses:**

Its alkaloids are Hypotensive, sedative and have tranquilising properties and are anti cancerous. It helps in relieving muscle pain, depression of central nervous system and wasp stings. It is used in case of nosebleed, bleeding gums, mouth ulcers and sore throats. It is also used internally for loss of memory, hypertension, cystitis, gastritis and enteritis, diarrhea and raised blood sugar levels.

**History of Vinca rosea:**

Peckolt, in 1910, described the use in Brazil of an infusion of the leaves to control hemorrhage and scurvy, as a mouthwash for toothache, and for the healing and cleaning of chronic wounds.

In Europe related species have been used for the proprietary suppression of the flow of milk [2]. In the British West Indies it has been used to treat diabetic ulcer [3] and in the Philippines has been reported as being an effective oral hypoglycemic agent [4]. More recently, Chopra et al. [2] have reported that the total alkaloids possess a limited antibacterial activity as well as a significant and sustained hypotensive action. The hypoglycemic and antibacterial activities have not been confirmed, although one of the alkaloids isolated from this plant, ajmalicine, has been reported to possess transient depressor action on arterial blood pressure [5].

**Herbal Drugs:**

It has been well recognized that allopathic drugs are not without danger as they exhibit severe toxicity on normal tissues. [1, 6] Therefore, worldwide research is going on to investigate the best effective antitumour agents from different sources. Recent pharmacological
researches revolve around the urgency to evolve suitable chemotherapeutic agents for the treatment of tumours (benign and malignant) without having toxic effects. [6,7] The indigenous system of medicine (Traditional Indian Medicine) has several medicinal plants with versatile medicinal properties that need detailed research for the development of herbal drugs. Herbal drugs having pharmacological anti tumor actions have been reported by many scientists. activities of several medicinal plants have been reported by various authors.[6-9,10-16] (mentioned in Table 1)

**Some Herbal sources of Drugs having Anti Tumor Properties:**

| Catharanthus roseus (Vinca rosea, Sadabahar) | Aglaia roxburghiana (Priyangu), | Abrus precatorious (Ghungchi) |
| Hygrophila spinosa (Talmakhana), | Solanum dulcamara (Kateli) | Ervatamia heyneana, |
| Ocimum sanctum (Tulsi), | Zingiber capitatum | Withania somnifera (Ashwagandha) |
| Wedelia calendulacea (Pila bhangra), | Vanda parviflora | Trigonella foenumgraecum (Methi), |
| Terminalia arjuna (Arjuna), | S. indicum (Barhanta), S. khasianum, S. surattense | Plumbago rosea (Chitra), |

**Alkaloids of Vinca rosea:**

Vinca rosea’s anti tumor properties are attributed to its major alkaloids Vincaleukoblastin(VLB) and leurosine. Two other alkaloids, vindoline and catharanthine also obtained from Vinca rosea, were devoid of antitumor activity singly or in equimolar concentrations, but have been postulated as the biogenetic precursors of VLB and leurosine. The experimental activity of a new clinically confirmed antitumor compound,Vincaleukoblastine (VLB) an alkaloid of Vinca rosea as the sulfate has been described. [17] VLB and leurosine are representatives of a new class of clinically active antitumor compounds which may interfere with the cellular metabolic pathways leading from glutamie acid to urea, and from glutamic acid to the citric acid cycle[18-22]
Action against P-1584:

The detection of activity against the P-1584 leukemia was considered particularly significant, owing to the fact that this tumor system has detected other clinically useful antitumor agents [23] and has been sensitive enough to study structure-activity relationship of active compounds which correlated with the clinical activity VLB has also been clinically confirmed [24]

Preliminary studies in vitro demonstrated that certain compounds were capable of reversing the growth-inhibitory activity of VLB against human monocytic leukemia cells. These compounds were coenzyme A, aspartic acid, tryptophan, a-ketoglutaric acid, ornithine, citrulline, arginine, and glutamic acid.[25]

Vincaleucoblastin:

The fractions from Vinca rosea were discovered to give interesting and, in some cases, profound activity against the P-1584 leukemia, an acute lymphocytic leukemia transplanted in DBA/~ mice. These findings led to a prompt phytochemical investigation in these laboratories which resulted in the obtaining of three new alkaloids: leurosine, virosine, and perivine.

Shortly after these compounds were obtained Noble, Beer, and Cutts 1 reported obtaining another new alkaloid as a sulfate from Vinca rosea. They suggested the name Vincaleukoblastine (VLB) for this compound. The most striking biological action of VLB was its leukopenic action in normal rats, which was used for its bioassay[23,26]. It was subsequently [27] demonstrated in both the Collip and Lilly Laboratories that VLB also markedly inhibited the P-1584 leukemia.

Leurosine:

Of the alkaloids studied, one isomeric with VLB --leurosine--has also shown a demonstrable retardation of the P-1534 leukemia. It has generally been of a lower order of activity than VLB, and less consistent. Of theoretical interest are the indole alkaloid, catharanthine, and the dihydroindole alkaloid, vindoline [28] Vindoline-like and catharanthine-like molecules each approximate one-half of the leurosine and VLB molecules. A solution containing equimolar proportions of these two alkaloids has an infrared absorption spectrum which approximates those of VLB and leurosine [29]. These compounds either singly or in an
equimolar solution have been devoid of any anti-P-1534 activity, as have all other pure alkaloids from this plant which have been tested. [30]

It has been reported by Cutts, Beer, and Xoble [4] that extracts of the plant *Vinca rosea*, when injected into rats, led to a marked fall in circulating leukocytes and to a depression of the bone marrow. Subsequently a new alkaloid, Vincaleukoblastine (VLB), was isolated [31] from such extracts; it caused marked hemopoietic effects [32] and affected the growth of experimental tumors [33]. The chemical and physical evidence indicated that VLB was a member of a new class of dimerical alkaloids which contain 1. CCTTS, J. H. Biological Effects of Extracts of *Vinca rosea*, both indol and dihydroindol moieties [17,26]

**Anti Diabetic Actions:**

**Diabetes mellitus:**

Diabetes mellitus is one of the common metabolic disorders with micro- and macrovascular complications that results in significant morbidity and mortality. It is considered as one of the five leading causes of death in the world [34,35].

**Phyto medicines for treating Diabetes mellitus:**

In modern medicine no satisfactory effective therapy is still available to cure diabetes mellitus [36]. There is increasing demand by patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents [37-39]. There are numerous traditional medicinal plants reported to have hypoglycemic properties such as Allium sativum (Garlic), Azadirachta indica (Neem), *Vinca rosea* (Nayantara), Trigonella foenum (Fenugreek), Momordica charantia (Bitter ground), Ocimum santum (Tulsi). Many of these are less effective in lowering glucose levels in severe diabetes.

**Anti hyperglycemic effect of *Vinca rosea***:

The two classes of active compounds in Vinca are alkaloids and tannins. Catharanthus roseus produces more than 100 monoterpenoids indole alkaloids (TIA) in different organs [40]. The leaves and stems are the sources of dimeric alkaloids, vinacristine and vinblastine that are indispensable cancer drugs, while roots have antihypertensive, ajmalicine and serpentine [41]. The leaves are used traditionally in various regions of the world including India,
West Indies as well as Nigeria to control diabetes [42]. The leaves have been known to contain 150 useful alkaloids among other pharmacologically active compounds.

Significant antihyperglycemic and hypotensive activity of the leaf extracts (hydroalcoholic or dichloromethane-methanol) have been reported in laboratory animals [43]. Fresh leaf juice of C. roseus has been reported to reduce blood glucose in normal and alloxan diabetic rabbits [44]. Leaves and twigs of Catharanthus roseus have been reported to have hypoglycaemic activity in streptozotocin induced diabetic rats [45].

**Fig. no.2 - showing the antihyperglycemic effects of Vinca rosea**

A study showed that alcoholic whole plant extracts of *Vinca rosea* at high dose (500 mg/kg) exhibited significant antihyperglycemic activity than whole plant extract at low dose (300 mg/kg) in alloxan-induced diabetic rats. These extracts also showed improvement in parameters like body weight and lipid profile as well as regeneration of cells of pancreas and so
might be of value in diabetes treatment. Further investigation is in necessary to determine the exact phytoconstituents (s) responsible for antidiabetic effect.[46]

It has been reported in a study that Administration of aqueous extracts of V. rosea flower and leaf have been found to regulate the blood sugar level in alloxan diabetic male albino rats. V. rosea therapy not only produced blood glucose homeostasis but also reversed changes in carbohydrate, protein, lipid metabolisms and metabolic and pathologic changes that took place in pancreatic islet cells, liver and kidney following a single dose (150 mg/kg body weight) of alloxan monohydrate. B-cell secretory activity resumed near-normalcy as evidenced by near-normal serum insulin concentration and electron-microscopic study proving that V. rosea manifests its beneficial activity through B-cell rejuvenation, regeneration and stimulation.[47]

**Anti Cancer effects:**

**Mechanism of Action:**

At pharmacologically active concentrations, most of the biochemical effects associated with exposure to the *Vinca* alkaloids are probably secondary to disruption of microtubules, although it is possible that drug-induced changes in lipid bilayers may alter some membrane-dependent processes. At high intracellular concentrations, these compounds induce formation of large crystalline aggregates that are composed of tubulin and drug.[48-50]

![Fig.no.3-Mechanism of action on Vinca alkaloids on microtubules](image)

Despite their many biochemical actions, the antineoplastic activity of the *Vinca* alkaloids is usually attributed to their ability to disrupt microtubules, causing dissolution of mitotic spindles...
and metaphase arrest in dividing cells.[51-58]. From the several effects of VLB on assembly of microtubules in vitro, it is generally assumed that the Vinca alkaloids disrupt microtubules by more than one mechanism.[59,60]

**At Lower Concentration:**

At low concentrations, VLB inhibits microtubule formation in a “substoichiometric” fashion in that assembly is blocked by binding of only a few molecules to high-affinity sites on tubulin heterodimers located at the ends of microtubules.[60]. It has been estimated that binding of Vinca alkaloids by this mechanism to only 1 to 2% of total tubulin could reduce microtubules by 50%.[61]

**At Higher Concentration:**

At higher concentrations, disassembly results from binding of VLB to tubulin heterodimers located along the microtubule surface, through stoichiometric interaction with Vinca-specific sites of reduced affinity and/or nonspecific ionic interaction [62,60]. Microtubules are dynamic, inherently polar structures that rapidly assemble and disassemble, depending on conditions at the ends[64-67]. In cells, one end is usually anchored to an organizing center and the other end may be either slowly growing by addition of tubulin heterodimers or rapidly shrinking[68]. Conversion between the two states, which is thought to be controlled by specialized proteins, occurs infrequently. At any given time, cells contain mixed populations of microtubules of different stability, and in at least one experimental system, there are differences among these populations in intrinsic sensitivity to Vinca alkaloids.[69-71]

**Pharmacological actions of Vinca Alkaloids:**

**IV Route of Administration:**

When administered by intravenous bolus injection, the normal route of administration, the Vinca alkaloids exhibit triphasic serum decay patterns in humans.[72-75] In adult cancer patients, the mean half-lives of the first two phases are about the same for VCR, VLB, vindesine (VDS), and VRLB (1–5 minutes and 1–2 hours), whereas that of the terminal phase differs by approximately four-fold for VCR (about 85 hours), VRLB (about 27–44 hours), VLB (about 25 hours), and VDS (about 24 hours). Following IV administration, the initial rapid
clearance of the **Vinca** alkaloids from plasma is due to uptake of drug by various tissues, particularly blood elements such as platelets[72,77-78]. The terminal phase of clearance from plasma represents the slow release of drug from various tissues where it has been sequestered, presumably through binding to tubulin. The range of values obtained for the terminal clearance phase, particularly with VCR, is large.[72,73] The greater potency of VCR has been attributed to prolonged exposures of sensitive tissues resulting from its slow clearance, relative to that of the other **Vinca** alkaloids.[79,73,74] VDS is equivalent to the plasma volume (5.4% of body weight), whereas VCR and VLB greatly exceed the plasma volume (32.8 and 70% of body weight, respectively)[73,74]

**Hepatobiliary Route of Administration:**

The **Vinca** alkaloids are excreted primarily by the hepatobiliary route.[80-82] Cancer patients with impaired liver function exhibit reduced clearance of VCR, resulting in higher steady-state concentrations of drug and prolongation of the terminal elimination phase.[83,84] In such patients a reduction in drug dosage is recommended to reduce VCR-related neurotoxicity.[85] The **Vinca** alkaloids are sometimes given by continuous intravenous infusion in an effort to maintain pharmacologically effective serum drug levels for a longer period. Although a variety of different schedules have been used, the administration of VCR, VLB, or VDS by infusion generally results in steady-state concentrations of drug that are higher than those achieved after intravenous bolus injection.[86-91] The pharmacokinetics of vinzolidine have been studied after either oral administration or intravenous bolus injection of tritium-labeled drug[92,93]. After oral administration, vinzolidine is rapidly absorbed, with an absorption half-life of 1 hour and a peak at 4 hours. The serum decay curve is biphasic, with half-lives of 10.5 and 172 hours. After intravenous administration, the pharmacokinetics of vinzolidine resemble those of VLB, except that the volume of distribution is much larger (about 15–20 times the blood volume). The terminal half-life for elimination of vinzolidine from plasma is about 23 hours.

**Adverse Effects:**

Exposure of nervous tissue to **Vinca**alkaloids inhibits axonal transport, causing neurotoxicity.[94,95] The **Vinca** alkaloids also inhibit secretory processes, apparently as a result
of perturbations in membrane trafficking with disruption of the cytoskeleton.[96] Platelets, which depend on the integrity of the peripheral ring of microtubules for their discoidal shape, become spherical after treatment with Vinca alkaloids.[97-98] These few examples illustrate that the Vinca alkaloids exert a variety of potentially cytotoxic effects that are unrelated to mitotic inhibition.

**Resistance to Vinca Alkaloids:**

In patients, drug effectiveness may also be a function of dose, route of administration, and pharmacokinetic factors, all of which compound the difficulties in interpreting whether cross-resistance between Vinca alkaloids occurs in clinical cancer. VCR-resistant acute lymphoblastic leukemia had been shown to be responsive to VDS, and several other studies support this finding.[99] VDS infusion was shown to be active in some patients who did not respond to bolus administration, and similar observations have been made with VCR and VLB. This suggests that, as in vitro, the degree of resistance between Vinca alkaloids may differ, and that dose and intensity of therapy may determine the response rate in Vinca-resistant disease.

**Conclusion:**

Vinca Alkaloids has set a milestone in the History of Modern Medicine. A little of its usage in medicine has been established by numerous studies still more of its hidden properties are yet to be explored. Some of its properties such as Antitumor effects, Antihyperglycemic effects along with its mechanism of pharmacological action has been described briefly in this Review. Hope this review will serve the purpose of aiding in future Research work to unleash the further components present in Vinca rosea.

**REFERENCES:**


17. GORMAN, M. Vinca Alkaloids IV. Structural Features of Leurosine and incalculeukoblastine,


