EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 10
Issue: 11
310-313
Year: 2023

PHARMACOLOGICAL EFFECTS OF VINCAMINE: AN OVERVIEW

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Article Received on 14/09/2023 **Article Revised on 05/10/2023** **Article Accepted on 26/10/2023**

ABSTRACT
Medicinal plants and herbs play a pivotal role in the treatment of various ailments as they contain several bioactive phytoconstituents. A large number of studies have explored the multiple pharmacological effects of several bioactive constituents from medicinal plants. Vincamine is one such phytoactive constituent that possesses multiple pharmacological properties. Vincamine has been reported to have diverse pharmacological effects including antioxidant, anti-inflammatory and anticarcinogenic effects. The present review highlights the pharmacological properties of vincamine and its mechanistic role, so far reported by various researchers.

INTRODUCTION
Traditional medicinal plants are a good source of novel bioactive constituents that contain multiple pharmacological effects. Vincamine is a monoterpenoid indole alkaloid obtained from *Catharanthus roseus*. This bioactive phytochemical has a variety of pharmacological and biological impacts including anti-inflammatory, antioxidant, anticoagulant, memory-improving, nootropic, hypoglycemic, hypolipidemic and vasodilator functions.[1,2] Vincamine is also well-known for its neuroprotective effects.[3,4] The structure of vincamine is given in the figure 1. This mini-review highlights the pharmacological effects of vincamine reported so far in both *in vitro* and *in vivo* research. For this particular review, the information on vincamine was collected from PUBMED resources and previous review articles as well as from cited references.

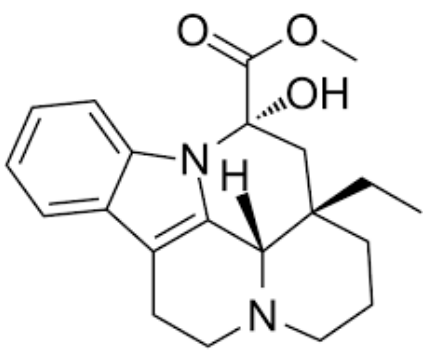

Figure 1: Structure of vincamine.

Anticancer effect of vincamine
Al-Rashed et al.,[5] explored the anticancer efficacy of vincamine in a human alveolar epithelial cell line A549. Vincamine showed its anticancer potential via inhibition of cell proliferation and increased fluorescence intensity caspase-3 activation as well as inducing ROS generation in A549 cells. Durai et al.,[6] reported the anticancer effect of vincamine in KB and Hep-2 cancer cells via its apoptotic potential. Vincamine significantly induced apoptosis in KB and Hep-2 cells via upregulating the caspase-3 and Bax expression as well as downregulating BCL-2 and mutant p53 expression. Han et al.,[7] investigated the influence of vincamine on amyloid-β 25-35 (Aβ 25-35) induced cytotoxicity in PC12 cells. Vincamine treatment efficiently improved cell survival, reduced apoptosis and cytotoxicity and lowered the concentrations of several oxidative stress indicators.

Antioxidant effect of vincamine
Durai et al.,[8] reported the antioxidant ability of vincamine by analyzing the various free radical scavenging assays. Vincamine significantly scavenged various free radicals in a dose-dependent manner under *in vitro* conditions.

Neuroprotective effect of vincamine
Sheref et al.,[1] reported the neuroprotective ability of vincamine in Parkinson's disease, induced by haloperidol in rats. They suggested that vincamine modulated striatal dopamine release and exhibited neuroprotective effects in haloperidol-induced Parkinson's disease rat models. Sanz et al.,[9] demonstrated that vincamine supplementation has disease-modifying effects in

Parkinson's disease models based on DJ-1 depletion in drosophila and human cells. Vincamine improved the viability of DJ-1-deficient SH-SY5Y human cells by decreasing apoptosis, boosting mitochondrial viability, and lowering the concentration of oxidative stress markers. Fischhof et al.,[10] demonstrated that vincamine has a beneficial therapeutic impact on the treatment of dementia patients. Vincamine was found to be therapeutically effective for dementia by modulating the Sandoz Clinical Assessment Geriatric Scale, Behavioral Rating Scale for Geriatric Patients and Short Cognitive Performance Test. Fayed[11] analyzed the concentration of brain trace elements in vincamine-treated rats. They concluded that the vincamine supplementation to rats caused a 50% decrease in brain Fe levels, which may reduce the Fe-mediated oxidative damage, particularly in older individuals. Abdel-Salam et al.,[12] reported the effect of vincamine on the enhancement of oxidative stress, inflammation and brain damage induced in rat brain by aluminium chloride ($AlCl_3$). They suggested that low doses of vincamine displayed anti-oxidant and neuroprotective effects whereas high doses showed pro-oxidant and proinflammatory properties. Li et al.,[13] demonstrated the neuroprotective ability of vincamine against non-arteritic anterior ischemic optic neuropathy in rats. They suggested that vincamine might have prevented retinal ganglion cell (RGC) death and decreased the number of apoptotic cells as well as significantly altered the P13K/AKT/eNOS signaling pathway. Ahmad et al.,[14] evaluated the anti-Alzheimer ability of vincamine using *in silico* approach. They concluded that vincamine could be used as a potent inhibitor of acetylcholinesterase for treating Alzheimer's disease.

Anti-diabetic effect of vincamine

Parlar Koprulu et al.,[15] examined the vincamine supplementation on testicular dysfunction in diabetic male rats. They reported that diabetes-related reproductive issues were prevented by vincamine. Nandini and Naik[2] pointed out the impact of vincamine on the metabolism of glucose and lipids in streptozotocin-induced diabetic rats. They suggested that vincamine explored its anti-diabetic and antihyperlipidemic effects via decreasing the level of glucose and serum lipid profiles as well as by increasing the activities of Superoxide dismutase (SOD), Catalase (CAT) and reduced glutathione (GSH) levels. Nasreena Shaban et al.,[16] demonstrated that vincamine has a modulating effect on the lipid profile and indicators of oxidative stress in streptozotocin-induced type 2 diabetic rats fed with a high-fat diet. They suggested that vincamine (30mg/kg b.w) exerted an antihyperglycemic effect by decreasing the lipids and decreasing the oxidative stress-related metabolic complications. Nasreena Shaban et al.,[17] explored the activities of the effect of vincamine on carbohydrate metabolizing enzymes in the liver and kidney of streptozotocin-induced diabetic rats. They suggested that vincamine supplementation stimulated the activities of carbohydrate metabolizing enzymes and played a crucial role in controlling glucose homeostasis. Du et al.,[18] investigated the β-cells protection and improvement of glucose homeostasis by vincamine treatment in both *in vitro* and *in vivo*. They concluded that vincamine inhibited the streptozotocin-induced apoptosis of β-cells via controlling the GPR40 / cAMP / Ca2+ / IRS2 / P13K / Akt signaling pathway.

Nephroprotective effect of vincamine

EI-Sayed et al.,[19] reported the nephroprotective molecular mechanism of vincamine against cisplatin-induced nephrotoxicity by analyzing the nephrotoxicity biomarkers, oxidative stress markers and inflammatory markers. They concluded that vincamine [40mg/kg p.o] has a significant role in nephrotoxicity via reducing the levels of both urea and creatinine and activation of the Nrf2/HO-1 signaling pathway as well as by inhibiting the TLR4-IFN-ɤ-CD44 cells inflammatory cascade. Shalaby et al.,[20] reported that vincamine showed its renoprotective effect against methotrexate-induced nephrotoxicity in rats via enhancing the production of Nrf2, by reducing HO-1 oxidative stress and through lowering the expression of inflammatory markers, NFkB and caspase-3 pathways. Fawzy et al.,[21] pointed out the use of vincamine together with pantoprazole to treat experimentally induced kidney ischemia/reperfusion injury. Vincamine demonstrated potent anti-inflammatory and anti-apoptotic properties in addition to pantoprazole in multiple dosages.

Hepatoprotective effect of vincamine

Dessouki et al.,[22] investigated the hepatoprotective efficacy of vincamine by examining the levels of serum and liver enzymes, inflammatory markers and p-JNK/p-ERK and NFkB pathways in the liver. They summarized that vincamine [10mg/kg b.w] showed its hepatoprotective potential by suppressing the oxidative stress, inflammatory markers, caspase-3, p-JNK/p-ERK and NFkB pathways in Tamoxifen-induced oxidative damage in rat liver.

Other pharmacological effects of vincamine

Alaaeldin et al.,[23] demonstrated that vincamine was protective against EMT in bleomycin-induced lung fibrosis by evaluating the apoptotic and TGF-1/p38 MAPK/ERK 1 signaling pathways. They reported the protective effect of vincamine reduced EMT by inhibiting the TGF-β1/p38 MAPK/ERK1/2 /TWIST/Snai1/slug/fibronectin/N-cadherin pathways as well as suppressing the p53/Bax/cleaved caspase 3 pathway. Erdo et al.,[24] showed the role of vincamine on voltage-gated Na+ channels both *in vivo* and *in vitro*. Vincamine served as a potent inhibitor of voltage-sensitive Na+ channels. Wu et al.,[25] reported the potential of vincamine against lipopolysaccharide-induced inflammation and oxidative stress in human corneal epithelial cells. They concluded that vincamine significantly inhibited both oxidative stress and inflammatory mediators' production via activation of

thioredoxin reductase activity. Li et al.,[26] investigated the role of vincamine on spiral ganglion neurons in guinea pig models of endolymphatic hydrops. They suggested that vincamine prevented the growth of endolymphatic hydrops in Meniere's disease by downregulating the Vasopressin/Aquaporin 2 signaling pathway. Lamar et al.,[27] reported the calcium antagonistic effects in various cerebral ischemia models through vincamine. In cerebral ischemia models, vincamine proved to be more effective and wider spectrum of activity than other calcium antagonists. Abdelkader et al.,[28] suggested that both retinal and optic nerve dysfunction was greatly improved with the combined treatment of vincamine, lutein and thioctic acid.

CONCLUSION

The present overview highlights the pharmacological effects of vincamine so far reported by various researchers. Vincamine has been reported to possess antioxidant, anticarcinogenic, anti-inflammatory, antidiabetic and neuroprotective effects. This review also pointed out the suggested mechanisms for its diverse pharmacological efficacies. The present overview of the pharmacological efficacies of vincamine concludes that vincamine can be used as a promising candidate for the treatment of various ailments including diabetes mellitus and neurodegenerative disorders.

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