ISSN: 0976-7126
Dubey *et al.*, 11(5):6590-6597, 2020

International Journal of Pharmacy & Life Sciences
Open Access to Researcher

Review on Vinpocetine

Anubhav Dubey*, Neeraj Kumar, Ashish Mishra, Yatendra Singh and Mamta Tiwari

1, Department of Pharmacology, Advance Institute of Biotech and Paramedical Sciences

Kanpur (U.P.) - India

Article info

Received: 12/03/2020

Revised: 29/04/2020

Accepted: 26/05/2020

© IJPLS

www.ijplsjournal.com

Abstract

Vinpocetine is a synthetic ethyl ester of apovincamine. It is extracted from the periwinkle plant. Vincamine is extracted from either the seeds of *Voacanga-Africana* or the leaves. Vinpocetine is an herbal supplement used to treat various neurological disorders such as Alzheimer's and Parkinson's disease. Vinpocetine has also anti-inflammatory, analgesics, antioxidant property and treat various thinking and memory problem. The drug has neuroprotective property thus it is used for memory impairment. Vinpocetine drug dilates blood vessels and promotes cerebral blood flow. Pharmacodynamics, Pharmacokinetic and adverse effects were discussed.

Keywords: Vincamine, neuroprotective, memory enhancement and cerebral blood flow Voacanga-Africana

Introduction

Vinpocetine was prepared under the trade name cavinton in 1978[1], vinpocetine widely used in Germany, Russia, Japan, Hungar for the treatment of the cerebrovascular related disorder. Vinpocetine is a semi-synthetic derivative obtained from vincamine alkaloid. Vincamine present in the aerial part of the vinca minor and plant belongs to the Apocynaceae family. Vinpocetine is approved by the European and British pharmacopoeias. Vinpocetine as well as vincamine are used in Europe, Japan and Mexico as a pharmaceutical agent for the treatment of cerebrovascular and cognitive disorders. [2]

Catecholamine levels were similarly increased 4-6 hours following the administration of vinpocetine. The authors also reported an inhibition of phosphodiesterase enzyme (PDE) suggesting a possible mechanism by which cerebral ATP levels seemed to be increased after administration of the compound. [3]

Modern lifestyle has raised life hope but also increase chronic harm full disease, therefore, increasing chronic Pharmaceutical usage, it is also called some time nootropic agent meaning cognition enhancer.

***Corresponding Author**
E.mail: anubhavdwivedi803@gmail.com

An analgesic role for vinpocetine show that it inhibits neuronal tetrodotoxin-resistant NAV1.18 with intraperitoneal (I.P) sodium channel current-induced calcium influx with (I.P) administration of vinpocetine reducing acetic acid visceral nociception, which is potentates by muscarinic, adrenergic, opioid receptor and blocked dependent on adenosine receptor. Vinpocetine drugs also inhibit formalin-induced paw flinching and inhibition of c- fos expression in the ipsilateral dorsal horn, when intraperineurally administered. Itblocks neuropathic pain through retrograde axoplasmic transport of nerve growth factor.[4] Although vinpocetine is not a microtubule inhibitor and its chemical structure shows no resemblance to that of vincristine, we found that at adequate concentration, vinpocetine inhibits retrograde axoplasmic transport of nerve growth factor (NGF), as shown by radiochemical studies. [5]

Vincamine is widely used as a neuroprotective agent for the prevention and treatment of central nervous system disorder of cerebrovascular origin.[6]In the U.S. vinpocetine supplements are marketed as sports supplements, brain enhancers, and weight loss supplements.[7, 8]

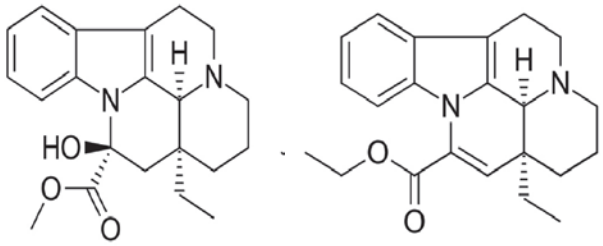
Vinpocetine is easily cross the blood-brain barrier (BBB), the therapeutic effect of vinpocetine high-capacity protect the neuronal cell from cytotoxic effects of inflammation oxidative stress and ion influx. Although vinpocetine inhibits phosphodiesterase-1(PDE-1) enzyme and anti-inflammatory effect present to be PDE-1 independent. [9]

Vinpocetine regulates the level of circulating TLRS in Parkinson's disease patients. Toll-like receptors (TLRs) are a class of proteins that play a key role in the innate immune system. Recent studies have shown that blockingTLR2 can reduce nuclear translocation of nuclear factor kappa-light-chain-enhancer of activated B cells. Therefore, TLRs provide promising candidates for the development of PD therapies. The findings that vinpocetine causes dilation of isolated cerebral arteries and improves the global cerebral blood flow suggest that cerebral circulatory effects may contribute to its Cerebral protective activity. [10,11]

Vinpocetine uses during pregnancy condition may harm the baby or result in miscarriage [12],the neuroprotective effects of vinpocetine related to blocking effects on the excitotoxicity effectsof glutamate and aspartate, and partly related to phosphodiesterase enzyme inhibition increases cerebral blood flow and decrease platelet aggregation.[13,14]

Chemistry of vinpocetine

Ethyl-Apovincamine 22-oate (Ethyl-Apovincaminate) is also known as vinpocetine, [15] Ethyl-Apovincaminatewas first synthesized by Lo¨rincz et al. from alkaloid vincamineobtained from the leaves of Vinca.[16]The IUPACName of vinpocetineEburnamenin-14-carboxylic acid ethyl esterand has molecular weight of 350.46g/m0l,Formula:$C_{22}H_{26}N_2O_2$ (Fig. 1), it is marketed in Hungary, Japan and several other countries for the treatment of cerebral diseases originating from vascular or cerebral metabolic disturbances,[17]the drug improves the cerebral use of oxygen and protects the brain cells against ischemic anoxia.



A **B**

Fig. 1: AVincamine B vinpocetine [18]

Marketed formulation of vinpocetin

There are the various formulation of vinpocetine was made various pharmaceutical company is given in the table, the recommended dose of vinpocetine is 15 to 30 mg in a day and sometimes increase the dose of vinpocetine to 40 Mg for special cases.

Table 1: Marketed formulation of vinpocetine

BrandName	PharmaceuticalCompanyName	DosageForm
Neurovin	Micro Labs Limited	5,10 mg
Cogvin	Intas Pharmaceutical Limited	5 mg tablet
Vinpotin	MJ-Bio-Pharm Private limited	5mg/ tablet and

		5mg/ml injection
Vinpocetine	SRS Pharmaceutical	10,20,30 mg vial injection

Mechanism of action

Vinpocetine has many pharmacological and biochemical activity, including cerebral vasodilatation, enhancing the tolerance of cerebral tissue to hypoxia and ischemia insults, anticonvulsant property, inhibitory effects on (phosphodiesterase), improving hematological flow property and inhibitory thrombolytic aggregation.

The neuroprotective effect of vinpocetine promotes the selective inhibition of calcium calmodulin-dependent $_{C}$GMP-PDE1, this inhibition may enhance intracellular $_{C}$GMP level in vascular smooth muscle leading to reduced cerebrovascular resistance and increased cerebral blood flow This property is also responsible for neuroprotection.[19]It could be hypothesized that vinpocetine may be useful for the treatment of Rheumatoid Arthritis (RA) due to its well established anti-inflammatory effects. [20, 21] Furthermore, a recent study has revealed that vinpocetine also has an ant hyperglycemic effect, [22] vinpocetine has antioxidant activity, and it prevents reactive free radical generation which contributed to the reduction of high glucose-induced oxidative damage. [23]

Pharmacology

Vinpocetine has many pharmacological and biochemical action is given below.

Inhibit the voltage-dependent sodium (Na^+) channel-Voltage-sensitive sodium channels (VSSC) play a fundamental role in the normal function of the CNS because they are responsible for the initiation and conduction of neuronal action potentials. Most of the energy demands coupled with the brainfunctional activity and used for ion transport and to restore the ionic gradients or degraded by excitation backto resting membrane potentials.[24]vinpocetine decreases DA and increased DOPAC in striatum isolated nerve endings, either under resting and under depolarized conditions.[25]

Antioxidant effect of vinpocetine-Oxygen-free radicals is a highly reactive chemical species generated in biologic systems during numerous physiologic and pathophysiologic processes. In physiologic circumstances, they play a role in cellular metabolism and cellular-defense systems. On the other hand, a large amount of oxygen-free radicals is highly toxic for tissues and cells because they can oxidatively modify and damage a variety of biologic systems. [26]

Epilepsy-Vinpocetine is a potent inhibitor of the epileptic cortical activity induced by the convulsing agents, pentylenetetrazole and 4-aminopyridine in the guinea pig in vivo, also we have shown that vinpocetine inhibits the release of several neurotransmitters triggered by the entrance of Nab,[27]vinpocetine and carbamazepine,valproic acid, whose mechanism of action mainly involves an increase in GABA nergic transmission was unable to decrease presynaptic ionic channels permeability in a broad range of concentrations.[28]The involvement of brain pre-synaptic Na^+channels in the mechanism of action of vinpocetine and carbamazepine is supported by the sensitivity of the increase in the internal concentration of Na^+ induced by 4-AP and veratridine depolarization to those anticonvulsants in cerebral isolated nerve endings.[29]The effects of two classic antiepileptic drugs (carbamazepine and phenytoin) a potential antiepileptic (vinpocetine) and a monoamine oxidase inhibitor (clorgyline) on the simultaneous changes (detected by HPLC) on Glue, Asp, dopamine, and DOPAC inside and outside striatal isolated nerve endings were investigated.[30]

Alzheimer's and Related Dementias-Alzheimer's disease (AD) is a progressive neurodegenerative disorder associated with cognitive and behavioral dysfunction. It is the leading cause of dementia in the elderly, [31]since dementia and particularly senile dementia of the Alzheimer type are a major and ever-increasing problem there is a strong need for therapeutic intervention. The clinical diagnosis of dementia is very difficult (especially beginning of disease not only in general medical practices but also in the hospital which provides the full range of modern diagnosis facility therefore essential for dementia so that careful evaluation of the patient made to ensure the homogeneity of the syndrome under-investigated.[32] Vinpocetine is a PDE1 inhibitor so that play an essential role in Alzheimer's,[33]it is well known that acetylcholine deficiency plays

an important role in the etiology of Alzheimer's disease. To study the effect of vinpocetine on acetylcholine (ACh) metabolism and assess its possible use in the therapy of Alzheimer's disease we have applied a model in which in a one-trial step-through passive avoidance task the memory functions of mice were impaired by scopolamine, an anticholinergic agent.[34]

Aging Process-Vinpocetine has been shown in animal studies to possess cerebral activating properties. In humans, reports indicate that vinpocetine improves cognitive processes and enhances recovery from cerebral ischemia. Thus both thepreclinical and clinical pharmacologic profiles indicate that vinpocetine may be a useful therapeutic agent for treating diseases characterized by cerebral impairments and cognitive or attention deficits. [35]

Vinpocetine protects liver against ischemia-refusion injury-Hepatic ischemia-reperfusion (IR) injury is an important clinical problem that complicates liver surgery and transplantation. The pathophysiology underlying hepatic IR injury is complicated, involving oxidative stress as well as inflammatory and apoptotic mechanisms. The neuroprotective effect of vinpocetine has been reported concerning IR injury in hippocampal neuronal cells both in vivo and in vitro, its role in protecting against IR injury in the liver. [36]

Vinpocetine Improves Neuronal Plasticity-Vinpocetine is an alkaloid extracted from the periwinkle plant and was tested as a neuronal plasticity enhancer and marketed as a "memory-booster. Vinpocetine treatment was shown long-term improve spatial memory in animal models and enhance performance on cognitive tests in humans. The cognitive enhancement function of vinpocetine comes from its inhibition of PDE type 1, which leads to an increase in cAMP and cGMP levels. These cyclic nucleotides can turn activate a series of kinases that phosphorylate the transcription factors cAMP response element-binding protein (CREB) and serum response factor (SRF), leading to the expression of plasticity-related genes. [37]

Anti-inflammatory activity-Vinpocetine is an inhibitor of phosphodiesterase type-1 (PDE1), which can lead to increases in cAMP and cGMP, thus initiating plasticity-related gene expression. Vinpocetine has a high affinity for the 18-kDa Translocator protein (TSPO) which is a biomarker of activated microglia and inhibits microglial proliferation through the NF κB/activator protein-1 (AP-1) pathway. It also suppresses the release of inflammatory factors. Vinpocetine suppressed the release of pro-inflammatory molecules by inhibiting the inhibitor of the IKK/NF- KB pathway after TNF-stimulation [38].Progression of the inflammation after ischemia-reperfusion injury, inflammatory cytokines activates nuclear transcription factor (NF-B) through toll-like receptor 4 (TLR4). NF-B signal transduction pathways promote target gene activation and induce neuronal apoptosis and even necrosis ultimately aggravating the cerebral disease however it remains unclear whether vinpocetine also suppresses mucus overproduction.[39, 40]

Vinpocetine inhibits the hearing loss induced by PTZ and AmikacinPTZ (Pentylenetrazole)-The auditory thresholds for 8 and 4 kHz tone frequencies were tested in all animals before the injection of PTZ and then 30 and 50 min after the injection of PTZ in the animals pre-injected with the vehicle or in the animals pre-injected with vinpocetine. PTZ in the animals pre-injected with the vehicle at the two-tone frequencies tested is lost in the animals pre-injected with vinpocetine. Vinpocetine alone (i.e. before the injection of PTZ) does not change the BAEP threshold. [41, 42]

Amikacin-Amikacin administered for 5 days at a dose of 450mg/kg/day markedly increased the auditory threshold for4 and 8 kHz tone frequencies in guinea pigs. This threshold increase was established at day 40 and lasted for more than 5 months, suggesting that the Amikacin regimen used caused a permanent (or at least long-lived) hearing loss in the animals. The animals also receiving vinpocetine, in contrast, maintained their auditory threshold values before treatment until the end of the experiment.[43]

Effect of Vinpocetine on Lipid Per oxidation-Atherosclerosis is the major trigger of myocardial infarction and strokes the leading causes of morbidity and mortality in developed countries. Cholesterol deposition in the artery wall plays a critical role in atherosclerosis. The extent of lipid per oxidation was determined by measuring thiobarbituric acid reactive substances (TBARS) expressed as malondialdehyde (MDA) using the thiobarbituric acid assay (TBA). The amount of

TBARS formed was calculated using a molar coefficient of 1.56 x 105mol -1 cm 1 and expressed as mole MDA/mg protein. The oxygen consumption was measured using a Clark-type electrode in a closed glass chamber equipped with magnetic stirring thermostatic at 30°C reactions were started by the addition of ascorbate-iron. The changes in 02 tensions were recorded in a potentiometric chart recorder and the oxygen consumption calculated assuming an oxygen concentration of 230 nmol O2/ml.Vinpocetine and Trolox were introduced in the incubation medium before the addition of ascorbate-iron. Blank experiments, in the absence of synaptosomes were performed to evaluate the oxygen consumption rate induced by acerbate/Fe 2^+ itself. [44]

Tinnitus/ Meniere's disease/ Visual Impairment- Tinnitus are the phantom perception of sound in the absence of overt acoustic stimulation. It is well known that chronic tinnitus is difficult to treat though lots of modalities are used for treatment. Current possibilities for chronic tinnitus treatment vary from neuroprotective substances, calcium-channel blockers, corticosteroids glutamate agonists, and thrombolytic drugs to intravenous or Intraperitoneallidocaine application vinpocetine (Cavinton) Pentoxifylline (Agapurin, Trental), or Piracetaminfusions. Vinpocetine Benzodiazepines also may provide relief, especially for patients with concurrent depression. In one study 76% of patients taking alprazolam had a reduction in the loudness of their tinnitus, whereas only 5% of the placebo group showed benefits also been starting to be useful in treating Meniere's disease and in vision impairment. [45, 46]

Vinpocetine effect on Parkinson's disease- Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease that is characterized by the irreversible loss of dopaminergic neurons in the substantianigraparscompacta (SNpc). The most general clinical sign of PD is tremor; it is present in 80-92% of patients. Rigidity is a common symptom not only for PD. However, it can be noticed in 67-99% of patients with this disease.[47] It is widely used as a neuroprotective agent that improves blood circulation, oxygen uptake and glucose utilization by the brain. Vinpocetine has been used in brain disorders and treatment of the signs of aging it can help improve cognitive function and short-term memory in both animals and humans,[48]In the brain from patients with PD an increased number of major histocompatibility complex (MHC) class II antigen [human leukocyte antigen-DR (HLA-DR)]-positive activated microglia which suggests an inflammatory process to occur in the brain in PD patients and the origin of cytokines most probably to be activated microglia.[49]

Cardio protective activity of vinpocetine- Cardiovascular diseases (CVD) is a common problem which is manifested by myocardial infarction due to deficient oxygen supply to cardiac muscles. Despite having a considerable amount of drugs available a search for better, safer, efficient and cost-effective drugs is always there. This study is a move in this direction. We have chosen vinpocetine a PDE1 inhibitor to assess its cardio protective role in this drug acute myocardial infarction (AMI) which is one of the .most common diseases in recent years, has been affected by several adverse living conditions of advancing technology. Myocardial infarction occurs as a result of a sudden interruption of blood flow with thrombotic occlusion of the previously narrowed coronary artery due to atherosclerosis. Vinpocetine has been documented that it has powerful antioxidant, anti-inflammatory and free radical scavenger effects. Consequently, it is possible to say that vinpocetine has a positive effect on cardiac function. [50, 51]

Pharmacokinetic of Vinpocetine

In human studies vinpocetine is absorbed from the small intestine and its active metabolites apovincaminic acid absorbed from the stomach. The pharmacokinetics of vinpocetine and its main metabolite apovincaminic acid were studied in the aged. Vinpocetine was eliminated with a mean half-life of 2.12± 0.51 h. Protein binding is about 86.6-±99.99%. The rate of vinpocetine absorption from the gastrointestinal tract is Rapid and peak plasma level is reached at about 1 hour after oral administration irrespective of dose food intake. Vinpocetine is more soluble in gastric pH (1.2) and intestinal PH (6.8). The vinpocetine is 1-2 hours and after 8-hour vinpocetine is eliminated from the body.[52-53]

Adverse Effects

Adverse effects of vinpocetine include flushing, nausea, dizziness, dry mouth, transient hypo- and

hypertension, headaches, heartburn and decreased blood pressure.[54,55] FDA stated 2019 warning that vinpocetine may cause a miscarriage or harm fetal development.[56]Vinpocetine has been implicated in one case in the induction of agranulocytosis serious condition in which granulocytes are markedly decreased. Some people have anecdotally noted that their continued use of vinpocetine reduces immune function. Commission E warned that vinpocetine-reduced immune function could cause apoptosis (cellular death) in the long term. Vinpocetine is dry mouth, transient hypotension, transient tachycardia, pressure-type headache and facial flushing. Slight reductions in both systolic and diastolic blood pressure with prolonged use of vinpocetine have been reported, as well as slight reductions in blood glucose. [57]

Conclusion

Vinpocetine first introduced to the market in under the trade name cavinton in 1978 (chemical works of Gedeon Richter Ltd, Budapest, Hungary) is a widely used compound in the treatment of cerebrovascular disorders. Vinpocetine smart drugs and smart nutrients with a wide variety of effects. And uses various treatments such as cerebrovascular disorder neurodegenerative disorder such as Parkinson's Alzheimer's disease, ototoxicity, analgesic and anti-inflammatory activity, cardioprotective activity hepatoprotective activity. Tinnitus Meniere's disease Visual Impairment, antioxidant activity, epilepsy activity, in the United States America vinpocetinesupplements are marketed as sports supplements, brain enhancers, and weight loss supplements. Vinpocetine has very few side effects and it has good pharmacokinetic and pharmacodynamics activity it is the best nutrients or drug for age-related memory impairment.

References

[1] Jha M.K, Rahman M.H and Sheikh Hasib: Vinpocetine a smart drug and a smart nutrient: a review. International Journal of Pharmaceutical Sciences and Research 2012; 2:346-352.

[2]Vora Saurabh C and Gujar Kishor N: Vinpocetine hype, hope and hurdles towards neuroprotection. Asian journal of Pharmaceutical Research and Development 2013; 4:17-23.

[3] Hindmarch I and Bhatti J. Z: Psychopharmacological effects of sertraline in normal. healthy volunteers. European Journal of Clinical Pharmacology 1988; 2:221–223.

[4] Ruiz-Miyazawa, K. W. et al: Vinpocetine reduces carrageenan-induced inflammatory hyperalgesia in mice by inhibiting oxidative stress, cytokine production and NF-κB activation in the paw and spinal cord. PLoS ONE 2015; 10(3):1–18.

[5] Csillik, B. et al: Mitigation of nociception via transganglionic degenerative atrophy
possible mechanism of vinpocetine-induced blockade of retrograde axoplasmic transport. Annals of Anatomy,2008; 190(2): 140–145.

[6] Ratra M, Sharma P and Gupta R: Neuroprotective effect of vinpocetine against 3-NP induced reduction of body weight and oxidative stress in rats. International Journal of Phytomedicine 201 3;(3): 362–369.

[7] Avula B. et al: Identification and quantification of vinpocetine and picamilon in dietary supplements sold in the United States 2015; 334–343.

[8] French J. M. T, King, M. D and McDougal O. M: Quantitative determination of vinpocetine in dietary supplements. Natural Product Communications2016; 11(5): 607–609.

[9]Ruiz-Miyazawa KW, Pinho-Ribeiro FA, Zarpelon AC, et al: Vinpocetine reduces lipopolysaccharide-induced inflammatory pain and neutrophil recruitment in mice by targeting oxidative stress, cytokines and NF-κB. Chemico- Biological Interactions 2015;237(5):9-17.

[10] Ping, Z. et al: Vinpocetine regulates levels of circulating TLRs in Parkinson's disease patients. Neurological Sciences 2019;40(1): 113–120.

[11] Krieglstein J and Rischik R: Protective Effect Damage of Vinpocetine Caused Brain by Ischemia. Japan. J. Pharmacol1991;56:349–356.

[12] Polgár M, Vereczkey L, Nyáry I: Pharmacokinetics of vinpocetine and its metabolite, apovincaminic acid, in plasma and cerebrospinal fluid after intravenous infusion. J Pharm Biomed Anal. 1985;3(2):131-139.

[13] Alkuraishy H M: management potential effects of vinpocetine on psychomotor performances and cognitive function capability in normal healthy volunteers randomized clinical trai. Journal of clinical Research and Health Care Management; 2012; 1:1-10.

[14] Feigin VL, Doronin BM, Popova TF, Gribatcheva E V, Tchervov D V: Vinpocetine treatment in acute ischaemic stroke: a pilot single-blind randomized clinical trial. Eur J Neurol. 2001;8(1):81-85.

[15] Khuble P, Juyal V: Vinpocetine a step towards memory enhancement. International Journal of Pharma Research and Development – Online 2011;(12):99-107.

[16] Bönöczk P, Gulyás B, Adam-Vizi V, et al: Role of sodium channel inhibition in neuroprotection: Effect of vinpocetine. Brain Res Bull 2000;53(3):245-254.

[17] Hammes W, Weyhenmeyer R: Quantitative determination of vinpocetine in human plasma by capillary gas chromatography-mass spectrometry. J Chromatogr B Biomed Sci Appl 1987;413(C):264-269.
[18] Vatsova M, Tzvetanov S, Drenska A, Goranscheva J, Tyutyulkova N. Improved gas chromatographic-mass spectrometric method for the quantitative determination of vinpocetine in human plasma. J Chromatogr B Biomed Appl 1997;702(1-2):221-226.
[19] Zhang Y shuai, Li J dong, Yan C: An update on vinpocetine new discoveries and clinical implications. Eur J Pharmacol 2018;819:30-34.
[20] Mandal A and Prabhavalkar KS: Evaluation of the efficacy of combination therapy of vinpocetine and withania somnifera methanolic.World Journal of Pharmacy and Pharmaceutical Science 2018;7(8):1295-1322.
[21] Alkuraishy HM, Al-Gareeb AI and Albuhadilly AK: Vinpocetine and pyritinol a new model for blood rheological modulation in cerebrovascular disorders a randomized controlled clinical study. Biomed Research International 2014;2:1-8.
[22] Ali Azza A, ASE-Z and ENAA-H: Evaluation of therapeutic efficacy of vinpocetine in adjuvant induced arthritis model in rats. Journal of Pain Management Pain Management & Medicine 2016;2(3):2-10.
[23] Wadie W, El-Tanbouly DM: Vinpocetine mitigates proteinuria and podocytes injury in a rat model of diabetic nephropathy. Eur J Pharmacol2017;814(8):187-195.
[24] Alkuraishy HM, Al-Gareeb AI and Albuhadilly AK: vinpocetine improves oxidative stress and pro-inflammatory mediators in acute kidney injury. International Journal of Preventive Medicine 2019; 79:192-221.
[25] Sitges M, Galván E and Nekrassov V: Vinpocetine blockade of sodium channels inhibits the rise in sodium and calcium induced by 4-aminopyridine in synaptosomes. Neurochem International journal 2005;46(7):533-540.
[26] Herrera-Mundo N, Sitges M: Vinpocetine and α-tocopherol prevent the increase in da and oxidative stress induced by 3-NPA in striatum isolated nerve endings. J Neurochem Journal 2013;124(2):233-240.
[27] Horvath B, Marton Z, Halmosi R, et al: In vitro antioxidant properties of pentoxifylline, piracetam, and vinpocetine. *Clinical Neuropharmacol*. 2002;25(1):37-42.
[28] Sitges M, Chiu LM and Guameros A, Nekrassov V: Effects of carbamazepine, phenytoin, lamotrigine, oxcarbazepine, topiramate and vinpocetine on Na^+ channel-mediated release of [3H] glutamate in hippocampal nerve endings. *Neuropharmacology* 2007;52(2):598-605.
[29] Gómez CD, Buijs RM and Sitges M: The anti-seizure drugs vinpocetine and carbamazepine, but not valproic acid, reduce inflammatory IL-1β and TNF-α expression in rat hippocampus. J Neurochem journal 2014;130(6):770-779.
[30] Sitges M, Sanchez-Tafolla BM, Chiu LM, Aldana BI, Guarneros A:Vinpocetine inhibits glutamate release induced by the convulsive agent 4-aminopyridine more potently than several antiepileptic drugs. *Epilepsy Research journal* 2011;96(3):257-266.
[31] Sitges M, Aldana BI and Chiu LM, Nekrassov V: Characterization of phenytoin, carbamazepine, vinpocetine and clorgyline simultaneous effects on sodium channels and catecholamine metabolism in rat striatal nerve endings. *Neurochem Re*search 2009;34(3):470-479.
[32] Dolu N, Gündüz S, Kara AY, Acer H, Tasan SN, Khan A: Is there treatment effect of vinpocetine on autonomic dysfunction in rats with alzheimer. *Asian J Pharm Clinical Res*arch 2017;10(2):89-91.
[33] Hindmarch I, Fuchs H-H and Erzigkeit H: Efficacy and tolerance of vinpocetine in ambulquant patient suffering from mild to moderate organic psychoasyndome. International Clinical Psychopharmacology 1991; 6:31-43
[34] Deshmukh R, Sharma V, Mehan S, Sharma N, Bedi KL:Amelioration of intracerebroventricular streptozotocin induced cognitive dysfunction and oxidative stress by vinpocetine - a PDE1 inhibitor. Eur J Pharmacol. 2009;620(1-3):49-56.
[35] Groó D, Pálosi É, Szporny L:Effects of vinpocetine in scopolamine-induced learning and memory impairments. Drug Dev Res. 1987;11(1):29-36.
[36] Notvest RR, Emrey TAand Inserra JJ. Effect of vinpocetine on age-related differences in brain function of aged fischer rats. Drug Dev Res. 1988;14(3-4):325-333.
[37] Zaki, Fahmy H, Abdelsalam and Mohsen R: Vinpocetine protects against liver ischemia-reperfusion injury. J Physiol Pharmacol 2013; 2-23
[38] Medina, Alexandre E: Vinpocetine as a potent anti-inflammatory agent. Proceedings of the National Academy of Sciences of the United States of America 2010; 22: 9921-9922.
[39] Zhang L, Yang L: Anti-inflammatory effects of vinpocetine in atherosclerosis and ischemic stroke: A review of the literature. Molecules. 2015;20(1):335-347.
[40] Wang H, Zhang K, Zhao L, Tang J, Gao L and Wei Z:Anti-inflammatory effects of vinpocetine on the functional expression of nuclear factor-kappa B and tumor necrosis factor-alpha in a rat model of cerebral ischemia-reperfusion injury. *Neurosci Lett*. 2014;566:247-251.

[41] Lee J-Y, Komatsu K and Lee B-C, et al. Vinpocetine Inhibits streptococcus pneumoniae–Induced up regulation of mucin MUC5AC Expression via Induction of MKP-1 Phosphatase in the Pathogenesis of otitis Media. J Immunology 2015; 194(12):5990-5998.
[43] Nekrassov V, Sitges M:Vinpocetine protects from aminoglycoside antibiotic-induced hearing loss in guinea pig in vivo. Brain Research 2000;868(2):222-229.
[44] Cai Y, Li JD and Yan C: Vinpocetine attenuates lipid accumulation and atherosclerosis formation. Biochem Biophys Res Commun. 2013;434(3):439-443.
[45] Santos MS, Duarte AI and Moreira PI, Oliveira CR: Synaptosomal response to oxidative stress effect of vinpocetine. Free Radic Research 2000;32(1):57-66.

[46] Hahn A, Radkova L, Achiemere G, Klement V and Alpini D, Strouhal J: Multimodal therapy for chronic tinnitus. International Tinnitus Journal. 2008;14(1):69-72.
[47] Seidman MD, Babu S: Alternative medications and other treatments for tinnitus f acts from fiction. Otolaryngol Clin North Am. 2003;36(2):359-381.
[48] Valeikiene V, Alekna V, Juozulynas A and Mieliauskaite D, Ceremnych J: Parkinson's disease the most common diagnostic mistakes in Lithuania. Cent Eur Journal Medicine 2009;4(3):304-309.
[49] Zaitone SA, Abo-Elmatty DM and Elshazly SM: Piracetam and vinpocetine ameliorate rotenone-induced Parkinsonism in rats. Indian J Pharmacol. 2012;44(6):774-779.
[50] Sawada M, Imamura K and Nagatsu T: Role of cytokines in inflammatory process in Parkinson's disease. J Neural Transm Suppl 2006;(70):373-381.

[51] Guven T, Sarihan M, Parlakpinar H, Vardi N and Tanbek K. Investigation of the protective and treatment effects of vinpocetine in myocardial infarctional with isoprotenol in rats. Med Sci | International Medical Journal 20171 1:2-8.
[52] Kaleem M, Haque SE: Evaluation of Cardioprotective Role of Vinpocetine in Isoproterenol-induced Myocardial Infarction in Rats. Journal of Pharmacy Research 2015;9(7):408-414.
[53] Miskolczi R, Vereczkey L, Szalay L and G6nd6cs C: Effect of Age on the Pharmacokinetics of Vinpocetine (Cavinton) and Apovincaminic Acid. Eur J Clin Pharmacology1987;33:185-189.
[54] Sozański T, Magdalan J and Trocha M, et al. Omeprazole does not change the oral bioavailability or pharmacokinetics of vinpocetine in rats.Pharmacological Reports 2011;63(5):1258-1263.
[55] National Toxicology Program *(September 2013)*. "Chemical Information Review Document for Vinpocetine (CAS No. 42971-09-5)" (PDF). U.S. Department of Health and Human Services. Retrieved December 28, 2018.

[56] Commissioner, *Office of the (2019-06-03)*. "Statement on warning for women of childbearing age about possible safety risks of dietary supplements containing vinpocetine. *FDA*. Retrieved 2019-06-04.

[57] Blumenthal M: The Complete German Commission E Monographs. American Botanical Council, Reprint Edition 1998.

Cite this article as:
Dubey A., Kumar R., Kumar S., Kumar N., Mishra A., Singh Y. and Tiwari M. (2020). Review on Vinpocetine, *Int. J. of Pharm. & Life Sci.*, 11(5): 6590-6597.
Source of Support: Nil
Conflict of Interest: Not declared
For reprints contact: ijplsjournal@gmail.com