Review

PHARMACOLOGICAL POTENTIAL OF VITEXIN

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ABSTRACT:

Vitexin is an apigenin flavone glycoside isolated from natural sources. It is considered as important as other flavonoids such as quercetin, rutin, kaempferol. In this review, we have documented some major occurrence and its major pharmacological activities such as anti-inflammatory, anti-oxidant, cardioprotective, anti-cancer, anti-nociceptive, anti-convulsant, memory enhancing potential and anti-diabetic activities. We have also drawn its 3D structure,total charge density by huckel using ChemDraw 3D and its theoretical chemical properties and analysis by ChemDraw.

KEYWORDS: Vitexin, Anti-inflammatory, Apoptosis, Cardioprotective,

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INTRODUCTION:

Vitexin is a flavonoid with poor water solubility commonly used to prevent heart diseases[1]. It is anapigenin flavone glycoside that utility of which has been demonstrated in several cardiovascular diseases. It is cardioprotective[2][3].It exhibited potent hypotensive, anti-inflammatory, anti-metastatic potential and anti-spasmodic properties. Hypotensive effect of Vitexin was attributed to its ganglion-blocking properties and anti-inflammatory effects to its anti-histaminic, anti-bradykinin, anti-serotonin properties and anti-oxidative[4][5][6].Vitexin has other potential such as anticonvulsant effects[7], enhancing memory retrieval[8], Anti-nociceptive effect[9], synergistically affect cell growth and apoptosis of colon cancer cells[10], induce apoptosis triggered by vitexin in U937 human leukemia cells via a mitochondrial signaling pathway[11] and anti-glycation activity[12]. It is known by many synonyms such as Apigenin-8-C-glucoside andOrientoside.5,7-dihydroxy-2-(4-hydroxyphenyl)-8-((2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yl)-4H-chromen-4-one) is the complete scientific name.

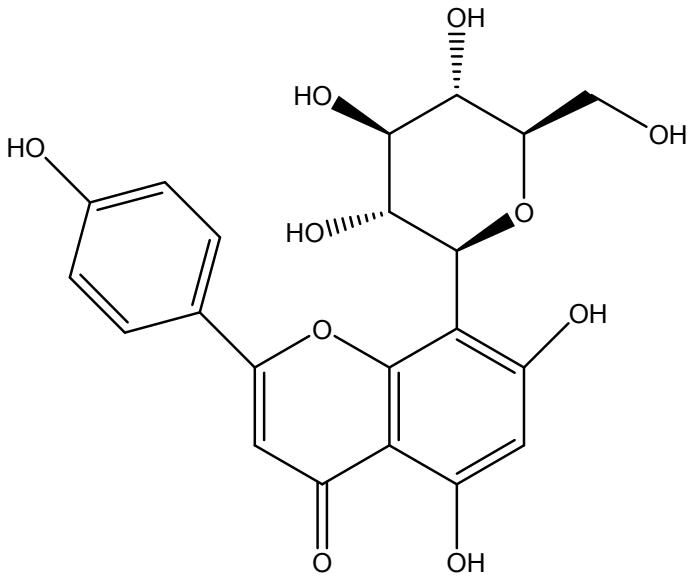


Figure 1: $C_{21}H_{20}O_{10}$

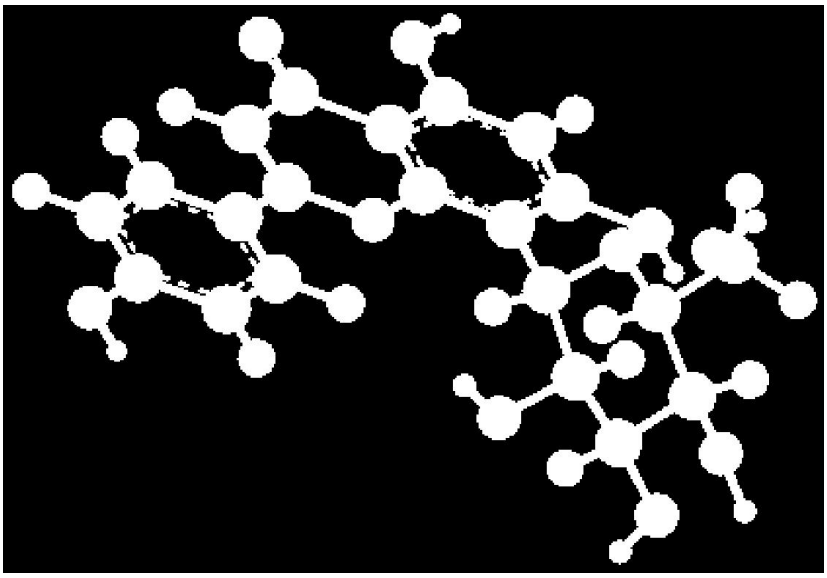
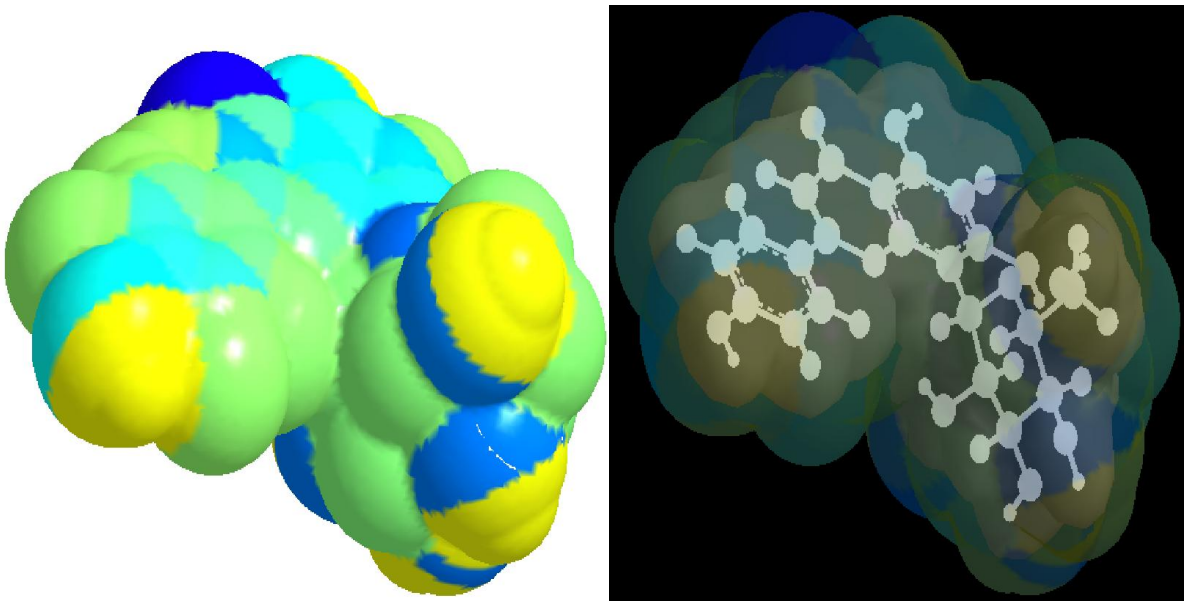


Figure 2: 3D Structure of $C_{21}H_{20}O_{10}$



(a)Solid **(b) Translucent**

Figure 3: Total charge density using Huckel

Properties	Values
Exact mass	432.11
Molecular weight	432.38
m/e	432.11 (100.0%), 433.11 (23.3%), 434.11 (4.6%)
Element analysis	C, 58.33; H, 4.66; O, 37.00
Boiling point	1496.39 [K]
Melting point	1125.97 [K]
Critical Temperature	1242.98 [K]
Critical Pressure	45.16 [Bar]
Critical volume	1033.5 [cm3/mol]
Gibbs Energy	-904.17 [kJ/mol]
Log P	Log P: -0.72
MR	107.77 [cm3/mol]
Henry's Law	38.18
Heat of Form	-1462.95 [kJ/mol]
CLogP	0.853993
CMR	10.5044

Table 1: Some important occurnace of Vitexin from Natural Product

Scientific Name	Part use	Reference
Acer palmatum	Leaves	[6]
Ficus deltoidea	Leaves	[13]
Clinacanthus nutans	Leaves	[14]
Mung bean	-	[12]
Crataegus monogyna	Top branches, flowers and leaves.	[15]
Trollius ledebouri	Flowers	[16]
Ficaria verna Huds.	Flower and leaves	[17]
hawthorn	Leaves	[18]
Achillea nobilis	Aerial	[19]
Buckwheat	seeds	[20]
Euterpe oleracea	pulp	[21]
Parkinsonia aculeata	Leaves	[22]
Passiflora incarnata	Flowers	[23]
Livistona chinensis	Fruit	[24]

PHARMACOLOGICAL ACTIVITIES:

Anti-inflammatory Potential:

Vitexin and isovitexin was evaluated by in vitro assays including rat lens aldose reductase (RLAR), human recombinant aldose reductase (HRAR), advanced glycation endproducts (AGEs), protein tyrosine phosphatase 1B (PTP1B), acetylcholin-esterase (AChE), butyrylcholinesterase (BChE), b-site amyloid precursor (APP) cleaving enzyme 1 (BACE1), and nitric oxide (NO), inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in lipopolysaccharide (LPS)-induced RAW 264.7 cells. Among them, isovitexin was found as the most potent inhibitor against RLAR, HRAR, AGE, AChE, and BChE while vitexin showed the most potent PTP1B inhibitory activity[25]. In general, flavones such as apigenin showed stronger inhibition of NO production than flavonols.Several flavonoid derivatives including apigenin, quercetin, and morin also inhibited NO production from LPS/ interferon (IFN)-activated C6-astrocytes [26].Apigenin, genistein, and kaempferol inhibited NO production by iNOS down-regulation[27]. Apigenin, genistein, and kaempferol strongly inhibited COX-2 induction by inhibiting nuclear transcription factor-$_k$B (NF-$_k$B) activation via inhibitor-B ($_k$B) kinase inhibition .Various flavonoid derivatives inhibited TPA-induced mouse ear edema when applied topically. The active flavonoids were mainly flavones/flavonols (having C-2,3-double bond), especially flavones such as apigenin and luteolin.The certain flavones/flavonols such as apigenin, quercetin, and morin showed significant, but weak anti-inflammatory activity (12 – 28% inhibition) by oral (100 mg/kg) and topical (2 mg/ear) routes[28].

Cardioprotective:

Lagenaria siceraria (Molina) Standl. (Cucurbitacae) (LS) has been reported to possess cardioprotective, antihyperlipidemic, and diuretic activities. To evaluate antihypertensive and cardioprotective effects of the *Lagenaria siceraria* fruit powder in N(G)-nitro-L-arginine methyl ester (L-NAME) induced hypertension in rats. Vitexin, orientin and isoorientin were detected in methanol extract of LS powder. The absence of necrosis, inflammation in the heart and significant reduction in serum cholesterol in LS and L-arginine treated rats indicated cardioprotective activity. Antioxidant activity of orientin and isoorientin appears to reduce the L-NAME induced damage. It is concluded that LS fruit possess antihypertensive and cardioprotective activity[29].Study of Vitexin on myocardial ischemia/reperfusion (I/R) injury in isolated rat hearts perfused with Langendorff apparatus. Treatment significantly enhanced coronary flow, and decreased the pathological scores of myocardium. Therefore, these results demonstrate that vitexin exhibits significant protective effect against myocardial I/R injury in isolated rat heart, which is related to inhibition of the release of inflammatory cytokines and the apoptosis of cardiac muscle cell via up-regulating protein expression of Bcl-2 as well as down-regulating Bax and and NF-κBp65[30]. It protects against cardiac hypertrophy via inhibiting calcineurin and CaMKII signaling pathways[3].Flavonoids and their in vivo metabolites are neuroprotective, cardioprotective and chemopreventive agents acting as hydrogen-donating antioxidants or modulators functioning at protein kinase and lipid signaling pathways. Treatments of human leukemia cells HL60 and their MDR-1 resistant subline HL60/VCR by flavonoids apigenin

(API), luteolin (LUT), quercetin (QU) and anticancer drug doxorubicin (DOX) are reported. Of all flavonoids used only QU treatments led in both cell lines to DNA fragmentation, cleavage of poly (ADP-ribose) polymerase (PARP), up-regulation of proapoptotic Bax and posttranslational modification (phosphorylation) of antiapoptotic Bcl-2. Cytochrome c and p21WAF1/CIP1 levels remained unchanged in these cells. Furthermore, treatments of both cell lines by QU and in its combined application with DOX increased phosphorylation of ERK, while Akt-1 and phosphorylated Akt-1 levels were not changed. All these events resulted in effective induction of apoptosis associated with down-regulation of P-glycoprotein in resistant cells. Presented results suggest that in human leukemia cells QU is a potent regulator of the cell apoptotic program associated with the modulation of several signaling molecules[31].

Anti-Cancer Potential:

Vitexin is a class of nature lignan compounds, whose action and anticancer effect is mediated by the mechanisms different from the classic lignans[32]. Vitexin have a potent effect on hypoxia- inducible factor-1α (HIF-1α) in rat pheochromacytoma (PC12), human osteosarcoma (HOS) and human hepa- toma (HepG2) cells. Vitexin inhibited HIF-1α in PC12 cells, but not in HOS or HepG2 cells. In addition, it diminished the mRNA levels of hypoxia-inducible genes such as vascular endothelial growth factor (VEGF), smad3, aldolase A, enolase 1, and collagen type III in the PC12 cells. It inhibited the migration of PC12 cells as well as their invasion rates, and it also inhibited tube formation by human umbilical vein endothelium cells (HUVECs). Interestingly, vitexin inhibited the hypoxia-induced activation of c-jun N- terminal kinase (JNK), but not of extracellular-signal regulated protein kinase (ERK), implying that it acts in part via the JNK pathway. Overall, these results suggest the potential use of vitexin as a treatment for diseases such as cancer[5].Vitexin, a lignan compound, has been shown to exert apoptotic actions on human breast cancer cell lines and to have anti-inflammatory activities[11].Vitexin-induced antitumor effect and cytotoxic activity is exerted through proapoptotic process, which is mediated by a decreased Bcl-2/Bax ratio and activation of caspases[32]. Vitexin-induced metastasis and apoptosis in human oral cancer cells, OC2 cells by possible existence of p53-dependent pathway. Vitexin decreased cell viability significantly. Meanwhile, the expression of tumor suppressor p53 and a small group of its downstream genes, p21 (WAF1) and Bax, were upregulated. The p53 inhibitor pifithrin-α (PFT-α) knockdown of the signaling of p53 led vitexin to lose its antitumor effect and inhibited the expression of p53 downstream genes, p21(WAF1) and Bax. Vitexin had anti-metastatic potential accompanied with increasing plasminogen activator inhibitor 1 (PAI-1) accumulation and decreasing matrix metalloproteinase-2 expression. The expression of p53 and its downstream genes p21 (WAF1) and Bax were enhanced by blocking the activation of p42/p44 MAPK in response to treatment with vitexin[33].

Anti-Oxidant Activity:

Vitexin inhibited superoxide radicals by about 70% at a concentration of 100 microg/mL and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals by about 60% at a concentration of 100 microg/mL[6].At high concentrations, ROS can cause severe damage to cellular structures and components including nucleic acids, pro- teins and lipids, thereby leading to apoptosis [34]. Malondialdehyde (MDA) is the most

abundant product of polyunsaturated lipid peroxidation. The reaction of MDA with thiobarbituricacidproducesthiobarbituric acid-reactive substances (TBARS) [35]. Vitexin is able to reduce the levels of MDA and TBARS and it also inhibits LDL oxidation. Vitexin's ability to enhance the viability of human umbilical vein endothelial cells induced by H_2O_2 is likely to be attributed by its high ROS scavenging activity in addition to its inhibition on lipid peroxidation[36].

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