REVIEW ARTICLE

# Nevadensin: Isolation, chemistry and bioactivity

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Nevadensin (5,7-dihydroxy-6,8,4'-trimethoxyflavone) has already established itself as a promising natural bioactive substance that bears the potential to become a novel "natural lead" in drug discovery programmes. The bioflavonoid exhibited a wide range of significant biological activities including hypotensive, anti-tubercular, antimicrobial, anti-inflammatory, anti-tumour and anti-cancer activities. This review deals with natural sources, isolation, chemistry and biological activities of the flavonoid in detail. The present resume is aimed to boost the ongoing researches on pharmaceutically potential natural "lead molecules" in drug discovery programmes.

**Key words:** Bioactivity, chemistry, isolation, natural sources, nevadensin

## INTRODUCTION

At the present scenario of scientific medicinal research, bioflavonoids are being considered much effective and useful due to their multidirectional therapeutic efficacies, and have already established as a class of therapeutically promising natural drugs and/or effective "lead molecules" in drug development and discovery processes.[1-3] Flavonoids comprise a large group of secondary plant metabolites, which are widely distributed throughout the plant kingdom, and are of importance and interest to a wide variety of physical and biological scientists. These naturally occurring polyphenolics exhibit a wide range of biological properties including antioxidant, anti-tumour, cytotoxic, enzyme inhibitory, antimicrobial, insecticidal and oestrogenic activities;[4,5] they are also used in the treatment of diabetes and cancer.[6-8]

Nevadensin is a natural bioactive flavonoid, isolated for the first time from *Iva* species by Farkas *et al*.;[9] other natural new sources for the compound have also been reported following this.[10-37] Nevadensin [systematic name: 2-(4-methoxyphenyl)-5,7-dihydroxy-6,8-dimethoxy-4*H*-1-benzopyran-4-one] is a pentaoxygenated flavone, i.e. 5,7-dihydroxy-6,8,4'-trimethoxyflavone [Figure 1]. This flavonoid molecule has been already shown to have a lot of pharmacological efficacies, and hence bears a promising potential of being a "natural lead" in the ongoing researches directed towards drug development and discovery. In this review, isolation, chemistry and biological activities of this important natural agent have been considered for discussion.

## NATURAL SOURCES

Exhaustive literature survey revealed that nevadensin is distributed in several medicinal plants as listed below:
*Acanthopanax trifoliatus* (Linn.) Merr. (syn. *Acanthopanax aculeatum* Seem.) (family: Araliaceae)[10]
*Baccharis* species (family: Asteraceae): *Baccharis nitida* Pers.[11] and *Baccharis grisebachii*[12]
*Biebersteinia orphanidis* (family: Geraniaceae)[13]
*Esenbeckia almawillia* Kaastra (family: Rutaceae)[14]
*Helianthus* species (family: Compositae): *Helianthus annuus* Linn.,[15,16] *Helianthus pumilus*[17]
*Hyptis albida* H.B.K. (family: Labiatae/Lamiaceae)[18]
*Iva* species (family: Asteraceae)[9]: *Iva nevadensis* M.E. Jones, *Iva acerosa* (Nutt.) Jackson
*Limnophila* species (family: Scrophulariaceae): *Limnophila aromatica*,[19,20] *Limnophila geoffrayi* Bon.,[21] *Limnophila rugosa* (syn. *Limnophila roxburghii*),[22] *Limnophila heterophylla* (Linn.) Druce[23]
*Lysionotus pauciflorus* (family: Gesneriaceae)[24-27]
*Ocimum* species (family: Labiatae/Lamiaceae)[28-32]: *Ocimum americanum* Linn. (syn. *Ocimum canum* Sims.), *Ocimum x citriodorum* Vis., *Ocimum basilicum* Linn., *Ocimum minimum* Linn.
*Ononis* species (family: Fabaceae/Leguminosae)[33-35]: *Ononis natrix* ssp. *hispanica*, *Ononis natrix* ssp. *ramosissima*
*Viguiera* species (family: Asteraceae)[36,37]: *Viguiera mollis*, *Viguiera procumbens*, *Viguiera bicolor.*

## EXTRACTION AND ISOLATION

Typical procedures as reported for the extraction and isolation of nevadensin from few of its natural sources are described herein.

**From *I. nevadensis***
Ground whole plants of *I. nevadensis* (740 g) were extracted with chloroform for 2 days; the crude gummy mass (22 g), obtained on removal of the solvent under reduced pressure was then chromatographed over

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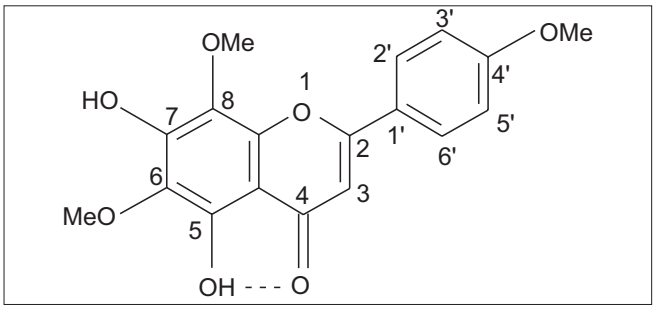



**Figure 1:** Nevadensin (5,7-dihydroxy-6,8,4'-trimethoxyflavone)

250 g of silicic acid. The column was eluted successively with benzene-chloroform (3:1) and benzene-chloroform (5:2). The fractions obtained on elution with benzene-chloroform (5:2) solidified on trituration with ether and were recrystallised repeatedly from benzene. This furnished nevadensin (0.2 g) which exhibited a double melting point of 186–188°C and 193–195°C (block).[9]

**From *I. acerosa***

Ground whole plants of *I. acerosa* (950 g) were extracted with chloroform for 2 days; the crude gummy mass (30.5 g) obtained on removal of the solvent under reduced pressure was then chromatographed over 225 g of silicic acid. The column was eluted with benzene. The fractions 22–26 (400 ml of benzene each) were solidified on trituration with ether and were recrystallised repeatedly from benzene. This furnished nevadensin (0.15 g) which exhibited a double melting point of 186–188°C and 193–195°C (block).[9]

**From *L. geoffrayi***

The pulverised, dried aerial plant materials (615 g) were extracted successively with *n*-hexane, chloroform and methanol in a Soxhlet apparatus. The chloroform extract (crude mass of 7.79 g) was chromatographed over silica gel (0.063–0.200 mm, 200 g), eluted with *n*-hexane-chloroform, chloroform and chloroform-methanol, with gradually increasing quantity of the more polar solvent. Fraction 11 was concentrated (4.99 g) and then chromatographed over silica gel (0.063–0.200 mm, 50 g) using chloroform and chloroform-methanol as eluents, with increasing percentage of the more polar solvent, to afford 13 subfractions; the 10th subfraction (110 mg) was further chromatographed to furnish nevadensin (15 mg).[21]

**From *L. heterophylla***

Air-dried defatted powered whole plants (1.5 kg) of *L. heterophylla* were extracted with petrol (60–80°C) in a Soxhlet apparatus for 56 hours. The extract was concentrated under reduced pressure and then subjected to column chromatography on silica gel (60–120 mesh, 200 g); the petrol:benzene (1:2) eluent afforded nevadensin as golden yellow needles (ethanol; 0.80 g).[23,38]

## PHYSICAL AND SPECTRAL PROPERTIES OF NEVADENSIN

Nevadensin (molecular formula: $C_{18}H_{16}O_7$) was obtained as golden yellow needles (from ethanol); $R_f$ value measured as: 0.70 ($CHCl_3$:EtOAc = 1:5). UV, IR, $^1$H-NMR, $^{13}$C-NMR, EIMS and 2D-NMR spectral properties of the compound are given below:

1. UV (ethanol): $\lambda_{max}$ 280, 335 nm; (+$AlCl_3$): 280, 310 (sh), 355 nm
2. IR (KBr) ν $cm^{-1}$: 3407, 3100, 2936, 2840, 1663, 1591, 1508, 1060, 1025
3. $^1$H NMR ($CDCl_3$, 300 MHz; TMS): δ 12.78 (1H, s, $C_5$-OH), 7.89 (2H, dd, *J* = 2.7 Hz, 11.7 Hz, H-2′ and H-6′), 7.045 (2H, dd, *J* = 3 Hz, 11.7 Hz, H-3′ and H-5′), 6.585 (1H, s, $C_3$-H), 4.04 (3H, s, $C_6$-$OCH_3$), 4.02 (3H, s, $C_8$-$OCH_3$) and 3.90 (3H, s, $C_{4'}$-$OCH_3$)
4. $^{13}$C NMR ($CDCl_3$, 75 MHz): δ 164.2 (C-2), 104.2 (C-3), 183.4 (C-4), 148.8 (C-5), 131.5 (C-6), 149.2 (C-7), 128.5 (C-8), 146.2 (C-9), 105.0 (C-10), 124.0 (C-1′), 127.8 (C-2′, C-6′), 115.0 (C-3′, C-5′), 163.1 (C-4′), 61.4 (8-$OCH_3$), 62.3 (6-$OCH_3$), 56.0 (4′-$OCH_3$)
5. EIMS (70 ev): *m/z* 344 ($[M]^+$), 329 (base peak), 316 $[M–CO]^+$, 315 $[M–CO–H]^+$, 314 $[M–2Me]^+$, 312 $[M–2Me–2H]^+$, 301 $[M–CO–Me]^+$, 212 and 132 (*retro*-Diels-Alder fragmented ion peaks), 197 and 132 (*retro*-Diels-Alder cleavage of mass fragment 329), 169 $[197\text{-}CO]^+$, 168 $[169\text{-}H]^+$, 153$[168\text{-}Me]^+$, 141 $[169\text{-}CO]^+$, 135 (fragmented ion peak), 126 $[141\text{-}Me]^+$, 113 $[141\text{-}CO]^+$, 107 $[135\text{-}CO]^+$, 101 $[132\text{-}OMe]^+$
6. 2D-NMR: Heteronuclear multiple-quantum coherence (HMQC) spectrum of nevadensin shows the expected one-bond heteronuclear ($^1$H–$^{13}$C) correlations; these are shown in Table 1.

## CHARACTERISATION

The present characterisation of nevadensin is based on the work of Brahmachari *et al*.[12] The dihydroxytrimethoxy flavone, $C_{18}H_{16}O_7$ ($[M]^+$ at *m/z* 344), responded positively towards flavonoid colour reactions and ferric chloride solution, and exhibited characteristic UV absorptions. The infrared absorption bands of the compound are also of the expected outcome, i.e. the flavonoid showed IR absorption bands for the presence of bonded hydroxyl function (3407 $cm^{-1}$), chelated α, β-unsaturated carbonyl attached with aromatic nucleus (1663, 1591, 1508 $cm^{-1}$) and methoxy group (s) (1060 $cm^{-1}$). The high resolution $^1$H NMR spectrum of the flavone displayed signals at (i) δ12.78 (1H,s) due to strongly bonded phenolic hydroxyl function, (ii) 7.89 (2H, dd, *J* = 2.7 Hz, 11.7 Hz, H-2′ and H-6′), (iii) 7.045 (2H, dd, *J* = 3 Hz, 11.7 Hz, H-3′ and H-5′), (iv) δ 6.585 (1H,s) attributed to $C_3$-H, (v) δ 4.04 (3H,s), 4.02 (3H,s) and 3.90 (3H,s) for three methoxyl functions.

The mass spectral fragmented ion peaks of the compound clearly suggest that two methoxyl and two hydroxyl functions are attached to the ring A, while the remaining methoxyl group is linked with the ring B, and unambiguously it must be placed at C-4′ as evidenced from the $^1$H-NMR spectral analysis. The appearance of intense green colour with ferric chloride imparted by the compound locates one of the hydroxyls at C-5 position[39] as also revealed from IR and $^1$H-NMR spectra. Again, the bathochromic shift of B and I by 20 nm (335→355) in the UV spectrum of nevadensin, in the presence of aluminium chloride that remained unchanged on the addition of hydrochloric acid, confirmed the presence of a hydroxyl function at C-5 and one of the methoxyls at C-6 position.[40,41] That the C-6 position is blocked by a methoxyl function is evidenced by its characteristic mass fragmentation pattern[42,43] as well as the negative response of the compound towards the colour reaction with *o*-dinitrobenzene.[9] A negative gossypetone reaction[44] suggested the presence of a methoxyl group at C-8 as well, and hence, the remaining hydroxyl group must be located at C-7 position, although there is no characteristic bathochromic shift of Band II in the UV spectrum upon addition of sodium acetate/ethanol, which is the peculiarity of nevadensin itself.[9] Hence, nevadensin must be formulated as 5,7-dihydroxy-6,8,4'-trimethoxyflavone. This structural formulation has been confirmed by $^{13}$C-NMR and HMQC spectral studies [Table 1]. The HMQC spectrum exhibited the expected heteronuclear cross peaks, for eight protonated carbons, showing one-bond heteronuclear correlations ($^1$H–$^{13}$C) between $C_{2'}$ and $C_{6'}$ protons at δ7.89 (2H, dd, *J* = 2.7 Hz, 11.7 Hz) with 2′ and 6′ carbons at δ127.8; $C_{3'}$ and $C_{5'}$ protons at δ7.045 (2H, dd, *J* = 2.7 Hz, 11.7 Hz) with 3′ and 5′ carbons at δ115.0; $C_3$-proton at δ6.585 (1H,s) with $C_3$-carbon at δ104.2, and the methoxy protons at δ3.90, 4.02 and 4.04 of three methoxyl functions, respectively, with the methoxyl carbons at δ56.0 ($C_{4'}$-$OCH_3$), 61.4 ($C_{8'}$-$OCH_3$) and 62.3 ($C_{6'}$-$OCH_3$).

**Table 1: $^{13}$C NMR data and HMQC results for nevadensin**

| C atom | $\delta_c$ value | HMQC |
|---|---|---|
| 2 | 164.2 | – |
| 3 | 104.2 | $\delta_{H-3}$ 6.585 |
| 4 | 183.4 | – |
| 5 | 148.8 | – |
| 6 | 131.5 | – |
| 7 | 149.2 | – |
| 8 | 128.5 | – |
| 9 | 146.2 | – |
| 10 | 105.0 | – |
| 1' | 124.0 | – |
| 2', 6' | 127.8 | $\delta_{H-2',6'}$ 7.89 |
| 3', 5' | 115.0 | $\delta_{H-3',5'}$ 7.045 |
| 4' | 163.1 | – |
| 8-$OCH_3$ | 61.4 | $\delta_H$ 4.02 |
| 6-$OCH_3$ | 62.3 | $\delta_H$ 4.04 |
| 4'-$OCH_3$ | 56.0 | $\delta_H$ 3.90 |

The proposed structure of nevadensin was also confirmed by its conversion experiment [Figure 2]. The parent compound on methylation with methyl iodide and potassium carbonate gave a dimethyl flavonoid derivative, which has been found to be completely identical with tangeretin (5,6,7,8,4'-pentamethoxyflavone) from the comparison of its physical and spectral data.[9]

## SYNTHESIS OF NEVADENSIN

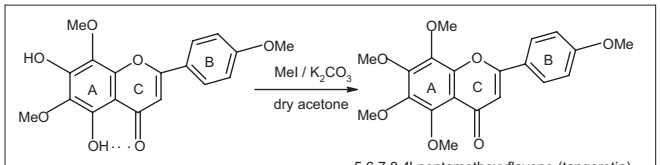
Farkas *et al*.[9] synthesised nevadensin starting with 2-hydroxy-4-benzyloxy-3,6-dimethoxyacetophenone (I).[45] Oxidation of I with potassium persulphate gave 2,5-dihydroxy-4-benzyloxy-3,6-dimethoxyacetophenone (II). Acetylation of II to III followed by the Baker-Venkataraman transformation led to 4-benzyloxy-2-hydroxy-5-(4-methoxybenzoyloxy)-3,6,4'-trimethoxydibenzoylmethane (IV), which was immediately cyclised to 7-benzyloxy-6-(4-methoxybenzoyloxy)-5,8,4'-trimethoxyflavone (V). Hydrolysis of V, followed by methylation of the hydroxyl function at C-6 as formed, furnished 7-benzyloxy-5,6,8,4'-tetramethoxyflavone (VI). Debenzylation and demethylation of VI at 20°C with aluminium chloride in dry ether ultimately afforded 5,7-dihydroxy-6,8,4'-trimethoxyflavone, which was found to completely identical with nevadensin. The schematic representation is given below [Figure 3].

## BIOLOGICAL ACTIVITIES OF NEVADENSIN

Nevadensin is a therapeutically potential natural flavonoid, and it was reported to exhibit a variety of biological activities. The significant pharmacological potentials of the bio-flavonoid are presented herein.

### Hypotensive Activity

Song *et al*.[46] studied the hypotensive effect of nevadensin in dog and cat models. In anaesthetised dogs and cats, intravenous, intramuscular or intraduodenal injections of




[$C_{20}H_{20}O_7$, m/z 372 $[M]^+$, mp 153-54$^0$ C, IR: 2936, 2845, 1663, 1592, 1507, 1458, 1028 cm$^{-1}$; PMR: d 3.90 (3H, s, Ar-$OCH_3$), 3.96 (6H, s, 2 x Ar-$OCH_3$), 4.04 (3H, s, Ar-$OCH_3$), 4.12 (3H, s, Ar-$OCH_3$), 6.61 (1H, s, $C_3$-H), 7.04 (2H, d, J = 9 Hz, $A_2B_2$ quartet, H-3' & H-5'), 7.04 (2H, d, J = 9 Hz, $A_2B_2$ quartet, H-2' & H-6')]

**Figure 2:** Conversion of nevadensin to tangeretin

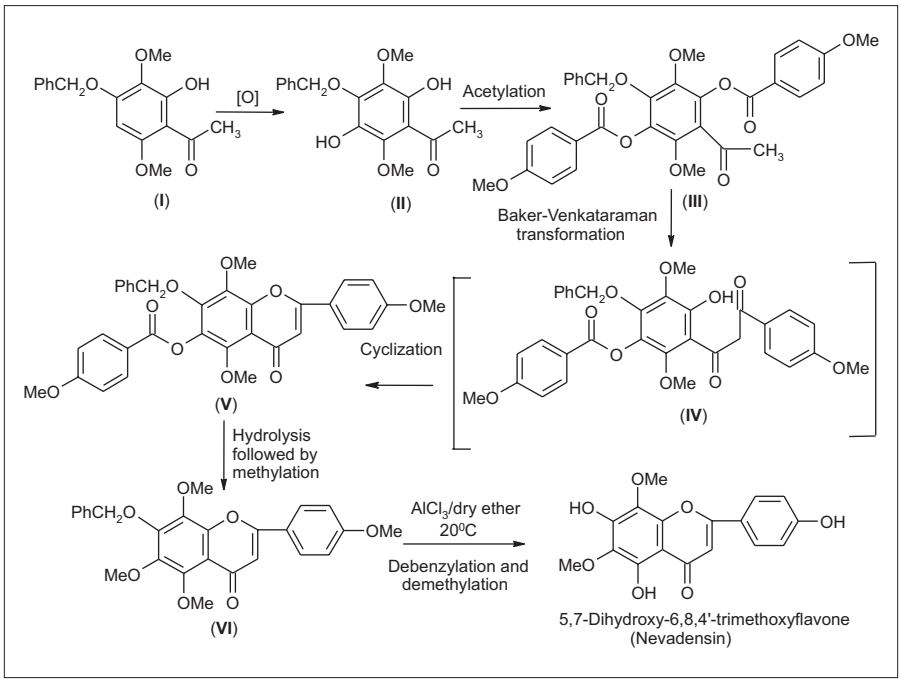



**Figure 3:** Synthesis of nevadensin[9]

the drug at doses of 2-40 mg/kg body weight lowered the blood pressure (BP) by 64 ± 7 mm Hg, retaining the heart rate and respiration unchanged. The BP gradually returned to its original level in next 2–4 hours. In dog model, the BP was found to be lowered more by the test compound (92 ± 7 mm Hg at a dose of 2.0 mg/kg) than by reserpine (62 ± 14 mm Hg at a dose of 1.5 mg/kg) or hexamethonium (78 ± 7 mm Hg at a dose of 2.0 mg/kg). The investigators also established that the hypotensive potential of nevadensin was similar to that of total alkaloids of *Rauwvolfia* (94 ± 7 mm Hg at a dose of 1.0 mg/kg). In this study, the mechanism of hypotensive action exerted by nevadensin appeared to be both central and peripheral in nature.[46]

**Anti-inflammatory Activity**

Reddy *et al*.[47] studied the anti-inflammatory activity of nevadensin in acute and chronic inflammatory rat model; carrageenan-induced rat paw oedema was compared at 0 and 3 hours with that of control (4% gum acacia mucilage). In tests for acute inflammatory activity, nevadensin showed significant inhibition by 45.28% ($P$<0.001) at a dose of 75 mg/kg body weight on oral administration.

**Anti-tubercular Activity**

Nevadensin and isothymusin (6,7-dimethoxy-5,8,4'-trihydroxyflavone), isolated from the chloroform extract of the aerial parts of *L. geoffrayi*, were reported to exhibit growth-inhibitory activity against *Mycobacterium tuberculosis* H 37Ra with equal minimum inhibitory concentration (MIC) value of 200 μg/ml;[21] however, the efficacy is relatively lower than those of the standard drugs (used during the experiment) rifampicin (MIC 0.003–0.0047 μg/ml), isoniazid (MIC 0.025–0.05 μg/ml) and kanamycin sulphate (MIC 1.25–2.5 μg/ml). But the flavone, nevadensin, was found to be more effective (MIC values: 100 μg/ml for nevadensin; 10 μg/ml for streptomycin used as standard) against the H 37Rv strain of *M. tuberculosis* as reported by Reddy *et al*.[47] The investigators suggested that the compound shows no toxicity up to 600 μg/kg orally in acute toxicity studies.[21] Baxter *et al*.[48] also evaluated the anti-tuberculostatic activity of nevadensin against *Bacillus tuberculosis* at a concentration of 0.2 mg/ml *in vitro.*

**Anti-tumour and Anti-cancer Activity**

Nevadensin was evaluated to inhibit markedly the growth of BEL-7404 cells – the T/C values [the ratio of cell number of treated (T) to controls (C)] were determined as 87.6, 80.6 and 34.9% at the doses of 1.0, 10 and 100 mg/ml, respectively.[49] The flavonoid was also reported to show moderate cytotoxic activity.[47] It showed 100% cytotoxicity at a concentration of 75 μg/ml both in Dalton's lymphoma ascites tumour and Ehrlich ascites tumour. Different concentrations of the drug containing nevadensin were used to test the cytotoxic activity. Dalton's lymphoma ascites tumour cells and Ehrlich ascites carcinoma cells were grown in the peritoneal cavity of Swiss albino mice. The compound was found to be more effective than wogonin (5,7-dihydroxy-8-methoxyflavone) that showed only 24.1% cytotoxicity in both the tumours at the same concentration. Hence, it can be argued that the methoxylated flavones possess moderate cytotoxic activity, which supports the view of Dong *et al*.[50] Nevadensin was also reported to possess moderate protein-tyrosine kinase (PTK) inhibitory activity against p40 with $IC_{50}$ value of 50 μg/ml, thereby expressing its anti-cancer potential.[51]

Estragole (a natural constituent of several herbs and spices including sweet basil) was found to be responsible for induction of hepatomas in rodent bioassays, an effect ascribed to estragole bioactivation to 1'-sulfooxyestragole (SULT, a proximate carcinogen), resulting in DNA adduct formation. Allhusainy *et al*.[52] established nevadensin as a constituent of basil, able to inhibit DNA adduct formation in rat hepatocytes exposed to the proximate carcinogen 1'-hydroxyestragole and nevadensin. The inhibition of SULT by nevadensin was incorporated into the recently developed physiologically based biokinetic (PBBK) rat and human models for estragole bioactivation and detoxification; the experimental results suggested that co-administration of estragole at a level inducing hepatic tumours *in vivo* (50 mg/kg body weight) with nevadensin at a molar ratio of 0.06, representing the ratio of their occurrence in basil, results in almost 100% inhibition of the ultimate carcinogen SULT, when assuming 100% uptake of nevadensin. Assuming 1% uptake, inhibition would still amount to more than 83%. Hence, this study pointed out a potential reduction of the cancer risk when estragole exposure occurs within a food matrix containing SULT inhibitors like nevadensin compared to what is observed upon exposure to pure estragole.[52]

**Anti-microbial Activity**

Nevadensin has also been found to have potent antibacterial activity against the test organisms – *Escherichia coli* and *Staphylococcus aureus*.[38] It showed strong cidal effect on *E. coli* by lysing the cells within 4 hours of treatment; the compound enhanced the activity of fructose bis-phosphatase, a gluconeogenic enzyme at sublethal dose, whereas it decreased the activity of phosphofructokinase and isocitrate dehydrogenase, the key enzymes of Embden-Meyerhof-Parnas and tricarboxylic acid cycle, respectively. Bacteriostatic as well as bacteriocidal effects of the test compound have been observed on *S. aureus*. The compound inhibits also the growth of a plant pathogenic fungus, *Alternaria solani*, but is unable to inhibit the growth of the yeast, *Candida albicans*. MIC of the compound for *E. coli* and *A. solani* were found to be 200 and 250 μg/ml, respectively.[53]

**Other Activities**

Brahmachari *et al*.[54] evaluated nevadensin for its cyclooxygenase-1 and 2 (COX-1 and COX-2) inhibitory efficacy by employing the COX catalysed prostaglandin biosynthesis assay *in vitro* method. The compound was found to exhibit moderate inhibitory activity against COX-1 and weak activity against the COX-2 with respective percent inhibition of 7.37 and 0.65% both at a dose of 10 μM.In addition, pharmacological experiments have shown that the flavonoid possesses expectorant and antitussive actions.[10]

Ganpaty *et al*.[55] evaluated free radical scavenging potential of gossypin and nevadensin using different *in vitro* systems including DPPH (1,1-diphenyl-2-picrylhydrazyl), nitric oxide, superoxide and hydroxyl radical assays; gossypin showed potent free radical scavenging properties, while nevadensin showed no significant efficacies in all these assays in comparison to those of the standard butylated hydroxyl toluene (BHT).

**Interaction of Nevadensin with Lysozyme Enzyme**

Lysozyme, a small enzyme also known as muramidase or *N*-acetylmuramide glycanhydrolase, protects us from the ever-present danger of bacterial infection by damaging bacterial cell walls.[56.57] Daojin *et al*.[58] carried out an interesting experiment on the interaction between nevadensin and lysozyme, using various spectrophotometric techniques including steady fluorescence, synchronous fluorescence, circular dichroism (CD) and UV/vis absorption. From their detailed study it was evident that nevadensin includes itself in the hydrophobic cavity of lysozyme *via* hydrophobic interactions. UV/vis measurements on the enzymatic activity of lysozyme in the absence and presence of nevadensin indicated that the interaction between nevadensin and lysozyme leads to a reduction in the activity of the enzyme. Furthermore, nevadensin binding to lysozyme had no influence on the molecular conformation of the enzyme.[58]

**Pharmacokinetic Study With Nevadensin**

Han *et al*.[59] studied the pharmacokinetic characteristics of nevadensin in animal models including rats, dogs and monkeys; drug [administered through both intravenous (*iv)* and intragastric gavage (*ig)* modes] concentrations in blood plasma of these animals with varying times along with measurement of the flavonoid excreted through urine were estimated thoroughly. Patterns of decline of the plasma level of the drug in the target animals conferred upon the body the characteristics of the two-compartment open model.[50] The investigators observed from the kinetic analysis that nevadensin was distributed fairly rapidly and eliminated rather quickly. It was noticed that absorption of nevadensin administered through intragastric gavage (*ig*) was very poor; however, when administered as an aqueous solution, the absorption was found to be fairly rapid but its bioavailability was low.[59] The same group of investigators also reported on the absorption, distribution and elimination of nevadensin in the rat, and the relationship between plasma concentration of the drug and its hypotensive effect.[60]

## CONCLUSIONS

Nevadensin has been evaluated to exhibit a variety of biological activities, and it demands for more detailed investigations on its pharmaceutical potentials. In-depth and systematic studies along with exact mode of action and safety evaluation for the compound are also necessary.

Studies on its semi-synthetic analogues are also to be considered. This resume has been compiled to boost the ongoing researches on pharmaceutically potential natural "lead molecules" in drug discovery programmes.

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