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An Overview of the Genus *Nardostachys*

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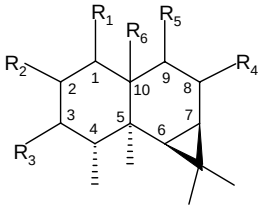
Nardostachys jatamansi, a medicinally important herb of Nepalese origin, has been used for centuries in the Ayurvedic and Unani systems of medicine. In combination with *Marsilea minuta* it is being used as an antistress and anticonvulsant drug and also finds use in the treatment of epilepsy. Recently, it has been reported that *N. jatamansi*, which plays an important role in protecting from cerebral ischemia and liver damage, is also used for the treatment of osteoporosis and hypercalcemia. The other member of the genus *Nardostachys*, *N. chinensis,* possesses antifungal and antimalarial properties. It is also used in the treatment of skin dysfunction. A short summary of the chemical constituents of the two species along with their physical and biological properties is reported.

Keywords: *Nardostachys jatamansi*, *Nardostachys chinensis*, Valerianaceae, chemical structure, biological importance.

Nardostachys jatamansi DC. is a high altitude plant, growing in the Himalayan foothills. Traditionally, *Nardostachys*, has been recommended in the Ayurvedic system of medicine for nervous and spasmodic symptoms, viz. heart palpitation, convulsion and hysteria [1-3].

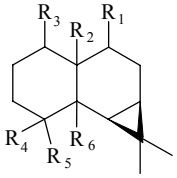
The genus *Nardostachys* belongs to the family Valerianaceae and consists of only two species [4]; *N. jatamansi* DC and *N. chinensis* Batal. In the Indian subcontinent the oil of *N. jatamansi* is used in several massage preparations. On the other hand, Gansong, a widely used analgesic herb in China, known as *N. chinensis* [5] is used for treating pain in the chest and abdomen [6]. The combination drug made from *Nardostachys jatamansi* and *Marsilea minuta* under the code name, Ayush 56, has been patented [7] by the Central Council for Research in Ayurveda and Siddha, Government of India, and purchased by National Research Development Corporation. An intensive search for the active constituents present in this genus revealed that the roots and rhizomes are potential sources of sesquiterpenes of common and lesser-known skeleta as discussed below.

(i) **Aristolane type:** Both species i.e., *N. jatamansi* and *N. chinensis*, contain several sesquiterpenes possessing the aristolane moiety (Figure 1). The compounds isolated are mentioned in Table 1.



Aristolane type sesquiterpene

Figure 1



Aristolane type sesquiterpene

Figure 2

Representatives of another type of aristolane sesquiterpene (Figure 2) isolated from this genus are shown in Table 2.

Spectral data of Aristolane Sesquiterpenes: The spectral data of Kanshone F (considered as a representative member of the aristolane skeleton) has been discussed [24].

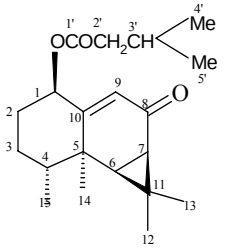
Table 1: Aristolane sesquiterpenes (Figure 1) isolated from the genus *Nardostachys*.

No.	Compound	Mol. Formula & Physical State	Ref.	Source	Substituents					
					R_1	R_2	R_3	R_4	R_5	R_6
i)	9,10-Dehydroaristolene	$C_{15}H_{24}$, b.p. 110°	[8, 9]	*N. jatamansi* (oil) *N. chinensis* (oil)	H	H	H	H	—	—
ii)	9-Aristolen-1α-ol (Nardostachnol)	$C_{15}H_{24}O$, m.p 85º	[8, 10-13]	*N. jatamansi* (roots) *N. chinensis* (oil)	OH (α)	H	H	H	—	—
iii)	1(10)-Dehydroaristolene (calarene)	$C_{15}H_{24}$	[8, 9, 11, 14-17, 48]	*N. jatamansi* (oil) *N. chinensis* (oil)	—	H	H	H	H	—
iv)	1,2,9,10-Tetradehydro-aristolene	$C_{15}H_{22}$	[8, 12]	*N. jatamansi* (oil) *N. chinensis* (oil)	—	—	H	H	—	—
v)	1(10), 8(9)-Aristoladien-2-one	$C_{15}H_{20}O$	[18, 19]	*N. chinensis* (oil)	—	=O	H	—	—	—
vi)	1(10)-Aristolen-9-one (Gansongone)	$C_{15}H_{22}O$	[13, 20]	*N. chinensis* (oil)	—	H	H	H	=O	—
vii)	1(10)-Aristolen-2-one	$C_{15}H_{22}O$	[10,14,18,19]	*N. jatamansi* (roots) *N. chinensis* (oil)	—	=O	H	H	H	—
viii)	9-Hydroxy-1 (10)-Aristolen-2-one (Debilon)	$C_{15}H_{22}O_2$	[21-23]	*N. chinensis* (roots & rhizomes)	—	=O	H	H	OH (α)	—
ix)	Kanshone F	$C_{20}H_{30}O_3$	[24]	*N. chinensis* (roots)	$OCOCH_2$ –i-pr (β)	H	H	=O	—	—
x)	Kanshone G	$C_{15}H_{24}O_2$	[24]	*N. chinensis* (roots)	—	OH (β)	H	H	OH (β)	—

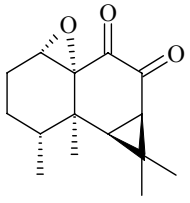
Table 2: Aristolane sesquiterpenes (another type) (Figure 2) isolated from these genera.

No.	Compound	Mol.Formula & Physical State	Ref.	Source	Substituents					
					R_1	R_2	R_3	R_4	R_5	R_6
i)	*β-Maaliene	$C_{15}H_{24}$	[8, 9, 17, 25 -27]	*N. jatamansi* (oil) *N. chinensis* (oil)	H	Me (α)	H	Me	—	—
ii)	*Maaliol	$C_{15}H_{26}O$ m.p. 103.5-105º	[25, 28]	*N. jatamansi* (oil) *N. chinensis* (rhizomes)	H	Me (α)	H	OH (β)	Me (α)	H
iii)	Calarenol	$C_{15}H_{25}O$	[11, 29]	*N. jatamansi* (oil)	H	—	—	OH (β)	Me (α)	Me (α)

*Later in 1967, Ruecker et al. [25] reported that these two compounds were not found in N. chinensis.



Kanshone F [24]
$C_{20}H_{30}O_3$
Figure 3



Kanshone C [20,30]
$C_{15}H_{20}O_3$; m.p. 136-137º
Figure 4

The olefinic proton at the α-carbon (C-9) of the α,β-unsaturated ketone appeared at δ 5.93 as a doublet of doublets. Two methine protons at C-1 and C-4 resonated at δ 5.55 and δ 1.88 respectively. H-6 and H-7 were discernible at δ 1.33 and δ 1.77 while the methyl protons (at C-12, C-13, C-14, C-15, C-4′, and C-5′) of the six-methyl groups resonated at δ 1.22, 1.26, 1.24, 1.09, 0.97, and 0.98 respectively.

The ^{13}C NMR spectrum of the compound showed the presence of an α,β-unsaturated carbonyl (C-8) at δ 195.9 and the ester carbonyl (C-1′) at δ 171.9. Two olefinic carbons (C-9 and C-10) were discernible at δ120.8 and δ 163.0. Two methine carbons (C-6 and C-7) linked to the isopropyl group appeared at δ 39.5 and δ 35.0 respectively. One methine (C-11) and two methyl carbons (C-12 and C-13) in the isopropyl group appeared at δ 24.4, 29.7, and 16.6 respectively.

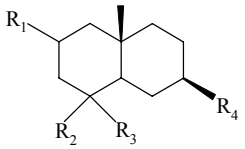
Interestingly, the abundance of aristolane derivatives [8] present in *N. chinensis* was greater than in *N. jatamansi*, except for 9-aristolen-1-ol (nardostachnol) as indicated in Table 3.

Besides the aristolane derivatives, kanshone C (1, 10-epoxy-8, 9-aristoladione), which is an epoxy derivative of aristolane (Figure 4), was isolated from *N. chinensis*.

Table 3: Comparative abundance of the compounds isolated from *Nardostachys chinensis* and *N. jatamansi*.

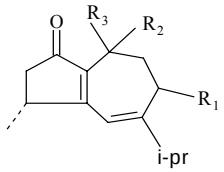
No.	Compound	*N. chinensis* (%) [8]	*N. jatamansi* (%) [8]
i)	9-Aristolen-1α-ol	8.0	69.4
ii)	9,10-dehydro Aristolene	2.1	0.2
iii)	1(10)-dehydro Aristolene	8.6	2.0
iv)	β-Maaliene	32.8	2.9
v)	1,2,9,10-Tetradehydroaristolene	13.1	2.9

(ii) **Eudesmane type:** Sesquiterpenes possessing this skeleton were mainly isolated from *N. jatamansi*. Until now, only one compound was reported from *N. chinensis* (Table 4) (Figure 5).



Eudesmane type sesquiterpene

Figure 5



Guaiane type sesquiterpene

Figure 6

(iii) **Guaiane type:** Investigation by a group of Japanese workers led to the isolation of several sesquiterpenes with the guaiane skeleton (Figure 6) from *N. chinensis*, viz. nardoguaianone A to K (Tables 5 and 6). Of these, nardognainone A to D were endoperoxides. Further research revealed the presence of two more endoperoxides isolated from the roots of *N. chinensis*, viz. nardoperoxide and isonardoperoxide, together with nardoxide, which contained an epoxy linkage (Figure 8) instead of the usual endo peroxy system (Figure 7).

Spectral data of Guaiane Sesquiterpenes: Spectral data of nardoguiaianones (E-I) have been considered as representative of the guaiane type sesquiterpenes [34]. From the spectral properties of the guaiane type compounds it was apparent that the two protons at C-3, i.e. 3α-H and 3β-H, resonated in the region δ 2.02-2.07 and δ 2.62-2.68 respectively as a pair of doublet of doublets. The methine proton at C-4 and the olefinic proton at C-6 appeared in the region δ 2.75-2.88 (ddq) and δ 5.75-6.33 (br t).

The –OH proton at C-8 in nardoguaianones E-G was discernible in the region δ 4.44-4.52, whereas the two methylene protons at C-8 in nardoguaianones H and I appeared in the region δ 2.43-2.45 (br. dd) and δ 2.33-2.36 (ddd). Six methyl protons at C-12 and C-13 in nardoguaianones E-G appeared in the region δ 1.15-1.18 (d) and δ 1.13-1.15 (d), whereas the methyl protons in nardoguaianone H and I showed signals in the region δ 1.14-1.42 (s) and δ 1.43-1.44 (s) respectively due to the presence of the –OH group at C-11. Six more methyl protons at C-14 and C-15 in all these compounds (nardoguaianones E-I) resonated in the region δ 1.13-1.26 and δ 1.44-1.49 respectively.

Table 4: Eudesmane type sesquiterpenes (Figure 5) isolated from the genus *Nardostachys*.

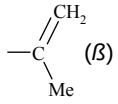
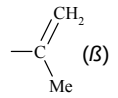
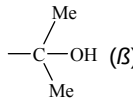
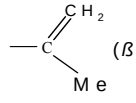
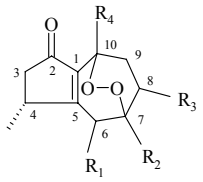
No.	Compound	Mol. Formula	Source	Substituents				Ref.
				R_1	R_2	R_3	R_4	
i)	Jatamol A	$C_{15}H_{24}O$	*N. jatamansi* (roots)	OH (α)	$=CH_2$	–		[31]
ii)	Jatamol B	$C_{20}H_{32}O_3$	*N. jatamansi* (roots)	$OCOCH_2C(Me_2)$ OH (α)	$=CH_2$	–		[31]
iii)	β-Eudesmol	$C_{15}H_{16}O$	*N. jatamansi* (roots)	H	$= CH_2$	–		[32]
iv)	Eudesm-11-en-2, 4-diol	$C_{15}H_{26}O_2$	*N. chinensis*	OH (α)	OH (α)	Me (β)		[33]

Table 5: Guaiane type sesquiterpenes (Figure 6) isolated from *Nardostachys chinensis.*

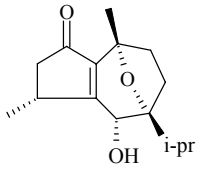
No.	Compound	Mol. Formula	Source	R_1	R_2	R_3	Ref.
i)	Nardoguaianone E	$C_{15}H_{22}O_3$	*N. chinensis* (roots)	OH (α)	OH (α)	Me (β)	[34]
ii)	Nardoguaianone F	$C_{15}H_{22}O_3$	*N. chinensis* (roots)	OH (β)	OH (β)	Me (α)	[34]
iii)	Nardoguaianone G	$C_{15}H_{22}O_3$	*N. chinensis* (roots)	OH (α)	OH (β)	Me (α)	[34]
iv)	Nardoguaianone H	$C_{15}H_{22}O_3$	*N. chinensis* (roots)	H	OH (α)	Me (β)	[34]
v)	Nardoguaianone I	$C_{15}H_{22}O_2$	*N. chinensis* (roots)	H	OH (β)	Me (α)	[34]
vi)	Nardoguaianone J	$C_{15}H_{22}O_2$	*N. chinensis* (roots)	H	Me (β)	OH (α)	[24]
vii)	Nardoguaianone K	$C_{15}H_{22}O_2$	*N. chinensis* (roots)	H	Me (α)	OH (β)	[24]

In the ^{13}C NMR spectrum the α,β-unsaturated carbonyl carbon showed chemical shifts ~δ 209.9-210.6. The four olefinic carbons (C-1, C-5, C-6, C-7) resonated in the region δ 140.3-142.1, δ 167.1-169.9, δ 113.1-117.4 and 164.4-167.9 respectively.



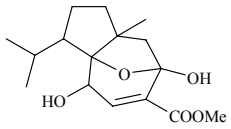
Guaiane type endoperoxide sesquiterpene

Figure 7



Nardoxide [35]
$C_{15}H_{22}O_3$

Figure 8



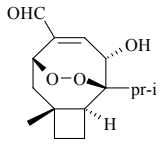
BR 606 [37]
$C_{16}H_{24}O_5$

Figure 9

However, the only epoxy sesquiterpene, named BR-606 (Figure 9), isolated from the roots of *N. jatamansi* has been frequently used for the treatment of osteoporesis [37].

Spectral data of guaiane type endoperoxide moiety: Spectral data of nardoperoxide and isonardoperoxide (considered as representative members of this skeleton) have been discussed [35].

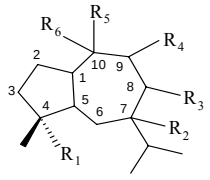
The two protons at positions 3 and 9 appeared in the range δ 2.1-2.8 and δ 1.7-2.1 respectively, while H-4 was generally observed in the region δ 2.8-3.2 (Figure 6). The two primary carbons at 3 and 9 resonated at δ 45-46 and δ 28-29 while the two tertiary carbons at 4 and 6 were observed around δ 32-37 and δ 69-73 respectively. The carbonyl carbon was observed in the low field region in the range δ 204-205. The two quaternary fused carbon atoms at C-1 and C-5 appeared in the region δ 143-145 and δ 177-179 respectively whereas the two peroxide linked carbons, i.e. C-7 and C-10, resonated in the range δ 83-84 and δ 78-80.



Nardosaldehyde [38]
$C_{15}H_{22}O_4$

Figure 10

In this context, it is important to note that the sesquiterpene containing an endoperoxy linkage, nardosaldehyde, was isolated from *N. chinensis* roots (Figure 10). This compound is different from all other guaiane type endoperoxy sesquiterpenes isolated from this species.



Guaiadiene type sesquiterpene

Figure 11

(iv) **Guaiadiene type:** Three sesquiterpenes containing a guaiadiene moiety were isolated from *N. jatamansi* (Figure 11, Table 7). Among these compounds, *nardostachysin* needs special mention. It is an ester of jatamansic acid (guaiadiene type sesquiterpene) and a bicyclic monoterpene alcohol.

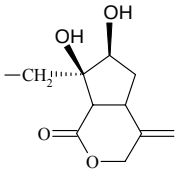
Table 6: Guaiane type endoperoxide sesquiterpenes (Figure 7) obtained from *Nardostachys chinensis*.

No.	Compound	Mol. Formula & Physical State	Ref.	Source	Substituents				Peroxo linkage
					R_1	R_2	R_3	R_4	
i)	Nardoperoxide	$C_{15}H_{22}O_4$ m.p. 129-130º	[35]	*N. chinensis* (roots)	OH (α)	i-pr (β)	H	Me (β)	O-O (α)
ii)	Isonardoperoxide	$C_{15}H_{22}O_4$	[35]	*N. chinensis* (roots)	OH (β)	i-pr (α)	H	Me (α)	O-O (β)
iii)	Nardoguaianone A	$C_{15}H_{22}O_4$	[36]	*N. chinensis* (roots)	OH (β)	i-pr (β)	H	Me (β)	O-O (α)
iv)	Nardoguaianone B	$C_{15}H_{22}O_4$	[36]	*N. chinensis* (roots)	OH (α)	i-pr (α)	H	Me (α)	O-O (β)
v)	Nardoguaianone C	$C_{15}H_{23}O_5$	[36]	*N. chinensis* (roots)	OH (α)	i-pr (β)	OH (α)	Me (β)	O-O (α)
vi)	Nardoguaianone D	$C_{15}H_{23}O_5$	[36]	*N. chinensis* (roots)	OH (β)	i-pr (α)	OH (β)	Me (α)	O-O (β)

Table 7: Guaiadiene type sesquiterpenes (Figure 11) isolated from the genus *Nardostachys.*

No.	Compound	Mol. Formula & Physical State	Ref.	Source	Substituents					
					R_1	R_2	R_3	R_4	R_5	R_6
i)*	Jatamansic acid	$C_{15}H_{22}O_2$ m.p. 123º	[15, 25, 39, 45, 46]	*N. jatamansi* (oil) *N. chinensis* (rhizomes)	H	—	—	—	—	COOH
ii)	Nardol	$C_{15}H_{26}O$ b.p. 120-125º	[11, 15, 47]	*N. jatamansi* (roots)	OH (α)	H	H	H	$=CH_2$	—
iii)	Nardostachysin	$C_{25}H_{34}O_6$ m.p. 192º	[48]	*N. jatamansi* (rhizomes)	H	—	—	—	—	COOR*

Where, R* =



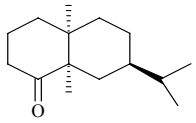
*Though jatamansic acid was reported earlier to be present in *N. chinensis*, its presence was contradicted by Ruecker *et al*. [25].

Spectral data of Guaiadiene Sesquiterpenes: Spectral data of nardostachysin and jatamansic acid (considered as representative compounds bearing the guaiadiene skeleton) have been discussed [39,48].

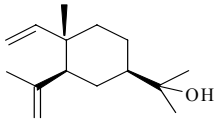
The two protons at the 7/5 ring juncture, i.e. H-1 and H-5, were discernible in the regions δ 3.0-3.1 and δ 1.65-1.75 respectively (Figure 10). The two-methine protons of the 7-membered ring, i.e. H-8 and H-9, resonated between δ 5.7-5.8 and δ 7.1-7.2 while the two-methyl and one-methine protons in the isopropyl group appeared at δ 1.07, δ 1.05, and δ 2.43 respectively. The ^{13}C NMR spectrum showed the presence of the acid carbonyl of jatamansic acid at δ 176.4 and the ester carbonyl of nardostachysin at δ 170.1. The two carbon atoms at the 7/5-ring juncture, i.e. C-1 and C-5 were observed at δ 45-47 and δ 43-45 while the two quaternary carbons of the 7-membered ring, i.e. C-7 and C-10, appeared in the regions δ 160-161 and δ 133-135 respectively. The three CH carbons of the 7/5-ring system (i.e. C-4, C-8, and C-9) were observed in the regions δ 38-40, δ 116-119, and δ 134-137 respectively.

(v) **Valerane and elemane type:** The roots and rhizomes of *N. jatamansi* were also found to contain valeranone and elemol as secondary metabolites. It is worth mentioning that valeranone possesses the valerane moiety whereas elemol is a member of the elemane group. The structures of the compounds have been shown in Figure 12.

So far, sesquiterpenes of common skeleta have been discussed. Several sesquiterpenes of uncommon skeleta, viz. nardosinane [13,19-21,23,25,30,42, 49-54] and nor-eremophilane [11,13,21,55,56] type were isolated from *N. chinensis*.



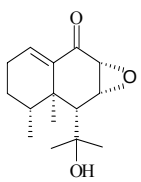
Valeranone (jatamansone) [11,25,26,28,39-41,42,43,44,48] $C_{15}H_{26}O$; b.p. 96-98º



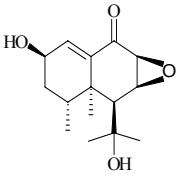
Elemol, $C_{15}H_{26}O$ [17,32] m.p. 48-51º

Figure12

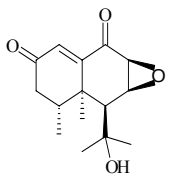
(vi) **Nardosinane type:** From the oil and gum of *N. chinensis* several sesquiterpenes possessing the nardosinane skeleton were isolated viz. isonardosinone, kanshone A-B, kanshone D-E, nardofuran, nardonoxide, nardosinone and nardosinonediol. An investigation of their structure revealed that isonardosinone, kanshone D-E,



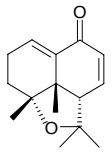
Isonardosinone [49,50] $C_{15}H_{22}O_3$



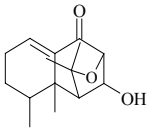
Kanshone D [49] $C_{15}H_{22}O_4$ m.p. 152-153º



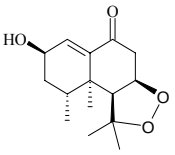
Kanshone E [49] $C_{15}H_{20}O_4$



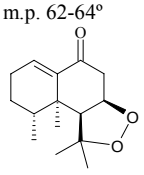
Nardonoxide [51] $C_{15}H_{24}O_2$ m.p. 62-64º



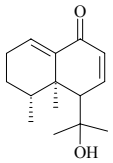
Nardofuran [49] $C_{15}H_{23}O_3$



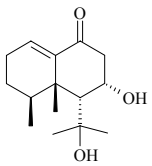
Kanshone B [52] $C_{15}H_{22}O_4$ m.p. 137-138º



Nardosinone [13,19-21,23,25,30,42,52,53] $C_{15}H_{22}O_3$; m.p. 108-110º



Kanshone A [21,23,52,54] $C_{15}H_{22}O_2$

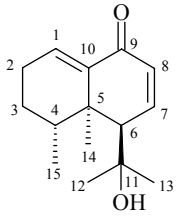


Nardosinonediol [13,21,49,50] $C_{15}H_{24}O_3$

Figure 13

nardonoxide, and nardofuran possessed an epoxy bridge whereas kanshone B and nardosinone contained a peroxy bridge (Figure 13).

Significant spectral data of the Nardosinane moiety: The spectral data of kanshone A (considered as a representative member of the nardosinane skeleton) has been discussed [52].

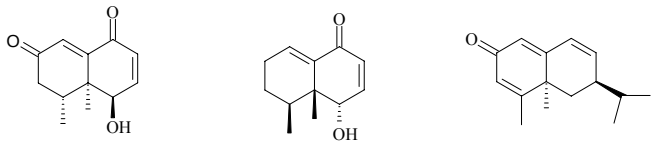


Kanshone A

In the ^{1}H NMR spectrum the protons of the methyl groups at C-4 and C-5 resonated at δ 1.02 and 1.08 respectively whereas the gem-dimethyls at C-11 appeared at δ 1.18 and 1.25. The methine protons at C-4 and C-6 appeared at δ 2.20 and 2.62 and the two olefinic protons at C-1 and C-8 were discernible at δ 7.0 and 6.16 respectively.

In the ^{13}C NMR study the carbonyl carbon appeared at δ 187.9, the two quaternary carbons at C-5 and C-10 at δ 42.0 and 141.6 respectively. The olefinic carbons at C-1, C-7, and C-8 were discernible at δ 137.2, 151.1, and 128.9.

(vii) **Noreremophilane type:** To date, three sesquiterpenoids having the noreremophilane moiety (Figure 14) have been isolated from this genus. Of these, narchinol A and desoxo-narchinol A were isolated from *N. chinensis* whereas nardostachone was obtained from *N. jatamansi* roots. Narchinol A and desoxonarchinol A belong to the tris-nor-sesquiterpenoid class.



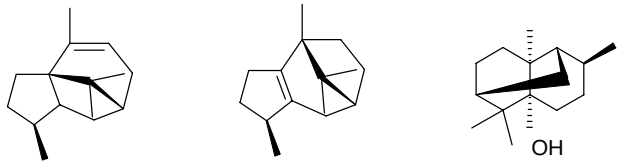
Narchinol A [55]
$C_{12}H_{14}O_3$
m.p. 146-148º

Des-oxo Narchinol A
[13,21]; $C_{12}H_{14}O_2$
m.p. 105-109º

Nardostachone [11,56]
$C_{15}H_{20}O$
b.p. 130-135º

Figure 14

(viii) **Patchoulane type:** Three sesquiterpenes of the rearranged patchoulane type skeleton, *viz*. α-patchoulene, β-patchoulene, and patchouli alcohol, were isolated from the roots of *N. jatamansi* and *N. chinensis*. The structures of these three compounds are shown in Figure 15.



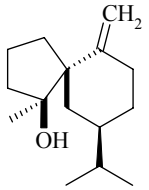
α-patchoulene [57]
$C_{15}H_{24}$
b.p. 53-54º

β-patchoulene
[17,57,58]; $C_{15}H_{24}$
b.p. 66-68º

Patchouli alcohol [57,58]
$C_{15}H_{26}O$
m.p. 55-56º

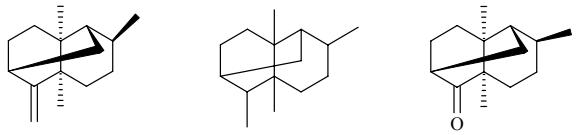
Figure 15

Along with all the sesquiterpenes mentioned, the presence of a spiranic sesquiterpene in the roots and oil of *N. jatamansi* was also reported. The structure of this spiro-sesquiterpene, spirojatomol, is shown in Figure 16.



Spirojatomol [41,43,59,60]
$C_{15}H_{26}O$
Figure 16

Sesquiterpenes possessing a bridgehead structure (Figure 17) were also isolated from the roots of *N. jatamansi*. A literature survey revealed the presence of seychellene, seychelane, and nor-seychelanone, all possessing [3, 3, 1] system.



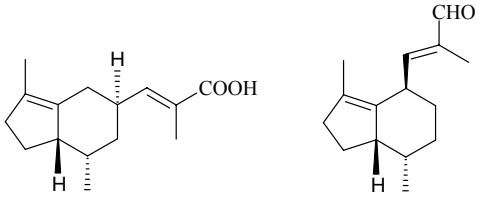
Seychellene [17,57,61]
$C_{15}H_{24}$; b.p. 70º

Seychellane [61]
$C_{15}H_{26}$

Norseychelanone [57]
$C_{14}H_{22}O$

Figure 17

Two sesquiterpenes, nardin (sesquiterpene acid) and valeranal (sesquiterpene aldehyde), were isolated from the roots of *N. jatamansi* (Figure 18).

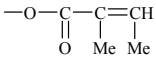


Nardin [62]; $C_{15}H_{22}O_2$
m.p. 133-134º

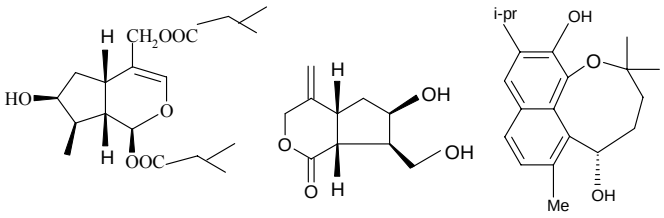
Valeranal [11,17]
$C_{15}H_{22}O$

Figure 18

Table 8: Coumarins (Figure 20) isolated from the genus *Nardostachys*.

Structural type	Compound	Mol. Formula & Physical State	Ref.	Source	Substituents	
					R_1	R_2
A	Angelicin	$C_{11}H_6O_3$, m.p. 137º	[32, 38]	*N. jatamansi* (roots)	H	—
A	Oroselol	$C_{14}H_{12}O_4$, m.p. 148-151º	[27]	*N. jatamansi*		—
B	Jatamansin	$C_{19}H_{20}O_5$, m.p. 97-98º	[27, 32]	*N. jatamansi*	_	 (α)
B	Jatamansinol (Lomatin)	$C_{14}H_{14}O_4$, m.p. 182º	[14, 15, 32]	*N. jatamansi* *N. chinensis*	_	OH (β)
C	7-Methoxy-8-isopentenyl coumarin	$C_{15}H_{16}O_3$, m.p. 81°C	Unpublished Result	*N. jatamansi* (roots)	OMe	—

Two new monoterpenes nardostachin and 6-hydroxy-7-(hydroxymethyl)-4-methylene hexahydro cyclopenta [c] pyran-1(3H)-one were isolated from the roots and rhizomes of *N. chinensis* (Figure 19).



Nardostachin [63] $C_{20}H_{32}O_6$

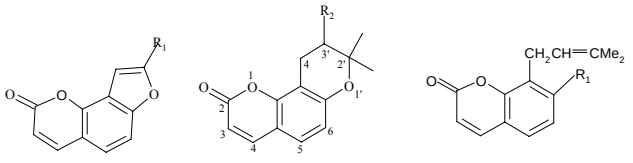
6-hydroxy-7-(hydroxy methyl) -4-methylene hexahydro cyclopenta [c] pyran-1- (3H)-one $C_{10}H_{14}O_4$ [23]

10-isopropyl-2,2,6-trimethyl-2,3,4,5-tetrahydronaptha [1,8-bc] oxocine-5,11-diol $C_{20}H_{26}O_3$ [23]

Figure 19

A new diterpene was isolated from the roots and rhizomes of *N. chinensis* (Figure 19) and characterized as 10-isopropyl-2, 2, 6-trimethyl-2, 3,4,5-tetrahydronaptha [1,8-bc] oxocine-5, 11-diol [23].

(ix) **Coumarins:** Besides terpenes, coumarin derivatives were also present in *N. jatamansi* [Table 8]. The coumarin derivatives isolated have been subdivided into furanocoumarins (Structure A) and pyranocoumarins (Structure B) (Figure 20). Later studies revealed the presence of osthol (Structure C). Jatamansinol is the only coumarin isolated from *N. chinensis* to date.



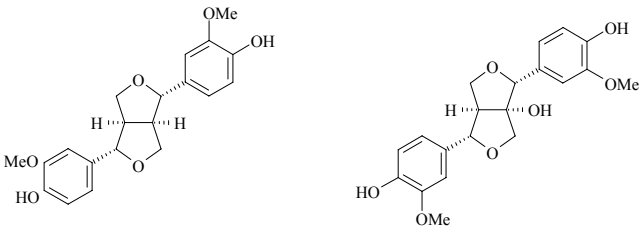
Structure A Structure B Structure C

Figure 20

(x) **Lignans and Neolignans:** Besides sesquiterpenes and coumarin derivatives, the presence of lignans and neolignans has also been reported from this genus.

The two-tetrahydrofuran lignans, isolated from the roots of *N. jatamansi,* were pinoresinol and 1-hydroxy pinoresinol (Figure 21).

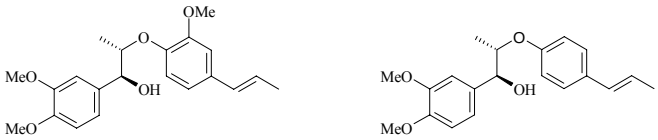
Another class of compounds i.e. neolignans were also isolated from the roots of *N. jatamansi* (Figure 22).



Pinoresinol 2,6-Bis- (4-hydroxy-3-methoxy -phenyl)-3,7-dioxobicyclo-[3,3,0] octane [64] $C_{20}H_{22}O_6$; m.p. 122º

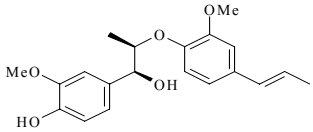
1-hydroxy pinoresinol 2,6-Bis-(4-hydroxy-3-methoxy-phenyl)-3,7-dioxobicyclo-[3,3,0]-octane-1-ol [64] $C_{20}H_{22}O_7$; m.p. 183-185º

Figure 21



Erythro-1- (3,4-dimethoxy phenyl) -2-(2-methoxy-4 (E)-propenyl phenoxy)-propan-1-ol [64] $C_{21}H_{26}O_5$

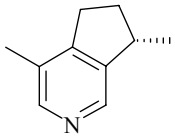
Virolin [64] $C_{21}H_{24}O_4$



Erythro-1- (4-hydroxy-3-methoxy phenyl)-2-(2-methoxy-4- (E)-propenyl phenoxy)-propan-1-ol [64]; $C_{20}H_{24}O_5$

Figure 22

Further literature survey revealed that only one alkaloid, i.e., actinidine (Figure 23), was obtained from the rhizomes of *N. jatamansi.*



Actinidine $C_{10}H_{13}N$ [65]
b.p. 100-103°

Figure 23

GC-MS studies of N. chinensis and N. jatamansi revealed the presence of several different types of compounds in trace amounts. These are listed in Table 9.

Table 9: Minor compounds from *N. jatamansi.*

No.	Compound	Ref.	No.	Compound	Ref.
1	α-Pinene	[15,17, 32]	22	Ledol	[15]
2	β-Pinene	[15,17, 32]	23	Cadina-1(10),6,8-triene	[15]
3	Δ^3-Carene	[32]	24	α-Copaene	[15]
4	β-Sitosterol	[10,11, 13, 32, 66]	25	Valencene	[15]
5	*n*-Hexacosanol	[11]	26	α-Selinene	[15]
6	*n*-Hexacosane	[11]	27	α-Cubebene	[15, 17]
7	*n*-Hexacosanyl arachidate	[11]	28	β-Copaene	[15]
8	*n*-Hexacosanyl isovalerate	[11]	29	7-Hexadecene	[15]
9	Isovaleric acid	[11]	30	Germacrene-D	[15, 17]
10	Formic acid	[15]	31	*cis*-β-Farnesene	[15]
11	Bornyl acetate	[15]	32	β-Elemene	[15]
12	Propionic acid	[15]	33	*trans*-Nerolidol	[15]
13	α-Terpineol	[15, 17]	34	Cycloprop(7,8) azulino(3a,4-b) oxirene	[15]
14	*p*-Cymene	[15, 17]	35	3,4-Dihydro-α-ionone	[15]
15	*n*-Hexane	[15]	36	(±)4-Terpeneol	[15]
16	*n*-Nonane	[15]	37	β-Selinene	[15, 17]
17	2-Ethylhexyl phthalate	[15]	38	β-Caryophyllene	[15]
18	β-Myrcene	[15, 17]	39	Cubebol	[15]
19	1,8-Cineole	[15]	40	α-Gurjunene	[15, 17]
20	Calamenene	[15]	41	γ-Gurjunene	[15]
21	Myrtenol	[15]	42	α-Humulene	[15, 17]

Compounds, such as ursolic acid [63], β-Sitosterol [13], oleanolic acid [13], ethyl-β-D-glucopyranoside [13] and β-ionone [17, 19] were ialso solated from *N. chinensis*.

Medicinal uses of *N. jatamansi* and *N. chinensis:* *N. jatamansi* has been prescribed in India since 800 B.C. for different ailments such as epilepsy, chest pain and palpitation [67]. Recently, it was observed that *N. jatamansi* had a protective effect on cerebral ischemia [68]. The exact mechanism of this effect is still uncertain. In cerebral ischemia there is an excessive accumulation of glutamate in extra-cellular fluid [69] and of sodium and calcium ions in the intracellular fluid [70]. *N. jatamansi* enhances the function of γ-amino butyric acid [71-73] by stimulating the γ-amino butyric acid neurons which antagonize the effect of glutamate and saves the neurons from cerebral ischemia. However, in ischemia, accumulation of free radicals as well as decreased function of free radical scavengers like Superoxide Dismutase (SOD) was also observed [74-76]. The antioxidant property of *N. jatamansi* protects the neurons from ischemic injury [77].

Jatamansone, a sesquiterpene ketone, isolated from the rhizomes of *N. jatamansi,* showed antiarrhythmic and anticonvulsant activities [44]. This substance has also been used in febrile delirium and delirium tremors. Jatamansone semicarbazone was found to possess antiestrogenic activity, which was reflected in its estrogen-antagonizing action on the uterus [78].

A novel compound, code name BR-606, isolated from *N. jatamansi* roots, has been found to be useful in the treatment of osteoporosis and hypercalcemia [37]. The presence of the epoxy linkage in this compound is probably the key factor (Figure 9) as this is known to inhibit bone sorption and help to correct osteoporosis and hypercalcemia.

The roots and rhizomes of *N. chinensis* (Japanese crude drug name "Kanshoko") are used as a sedative and an analgesic in oriental medicines [24].

N. chinensis is known to be rich in terpenoids. Some of these possess antimalarial activity. Although, a number of medicines such as chloroquine and quinine are frequently used for the treatment of malaria, the rapid development of drug resistance poses a serious problem. Therefore new medicinal agents are required to overcome the drug resistance as well as to control epidemics caused by malarial parasites. During the search for new types of antimalarial compounds from plants, nardosinone [25] (Figure 13), an important constituent of *N. chinensis* roots, was found to exhibit antimalarial activity against *Plasmodium falcifarum* (EC_{50} 4.5 x 10^{-6} M). Further

research on this plant revealed the presence of three more guaiane type sesquiterpenoids, viz. nardoperoxide [35], isonardoperoxide [35] and nardoxide [36] (Table 6, Figure 7), all of which showed strong antimalarial activity. Further attempts to isolate antimalarial drugs led to the isolation of four guaiane-type endoperoxides, nardoguaianone A-D [36] from the roots. It was subsequently established that all these compounds have stronger antimalarial activity than the well-known antimalarial chloroquine. It is worthwhile to mention that nardoguaianone E to K [24, 34] (Table 5) does not exhibit any antimalarial activity. A close examination of their structures and the lack of the antimalarial activity of nardoguaianones E to K revealed that only those compounds having peroxo or oxo linkages exhibit antimalarial activity.

Among these antimalarial sesquiterpenoids, nardoperoxide, isonardoperoxide, nardoxide and nardosinone showed cytotoxicities against FM3A and KB cells [35]. Malaria infected cells exhibit specific cytotoxic effects on treatment with these compounds and thereby these can be considered to be effective in the treatment of the disease.

From the above discussion it can be inferred that the genus '*Nardostachys*' is rich in several classes of compounds viz. sesquiterpenes, coumarins, lignans and neo-lignans. The never-ending requirement for the exploration of the rich medicinal armamentarium, with which nature has endowed mankind, stimulated the impetus to undertake in depth study of this genus. This resulted in the development of Ayush 56 [7] the combination-drug with *Marsilea minuta*, which finds use as an anti-stress, anti-convulsant and rehabilitation drug. The discovery of this combination-drug is a landmark in developing "alternate lines of treatment" leaving no side effects.

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