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Chemical Constituents of the Himalayan Yew, A Review†

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Abstract – A large number of chemical constituents have been reported from the Himalayan yew [*Taxus baccata* (Linn) or *T. wallichiana* (Zucc)]. These constiuents are mainly taxoids and phenolics. Taxol, a lead anticancer agent, is the most important constituent. Other compounds have also been found to possess interesting biological properties. The literature concerning the chemistry and bioactivity of the constituents of the Himalayan yew has been briefly reviewed.

Key words – Himalayan yew, *Taxus baccata* (*T. wallichiana*), taxoids, phenolics, chemistry, bioactivity.

Introduction

The yew plants (*Taxus* species, family Taxaceae) have gained a significant attraction in recent years because of their biologically active chemically complex metabolites. Taxol (1) (Wani *et al.*, 1971), an exceptionally promising cancer chemotherapeutic agent, was originally isolated from the bark of *T. brevifolia* but recently the compound has been reported (Das *et al.*, 1996d) from different parts of various other yew plants. In India the yew plants are available in the Himalayan region. The Himalayan yew is often referred to as *T. baccata* (Linn) but some authors have recently described it as *T. baccata* subsp. *wallichiana* (Zucc) or simply as *T. wallichiana* (Zucc) (Chattopadhyay and Sharma, 1995b; Appendino, 1995). The plants are found (Chopra *et al.*, 1956 and Bahoray *et al.*, 1979) in the temperate Himalayas at altitudes between 1800 and 3300 m. They are slow growing long lived evergreen trees, usually 6 m or so in height and about 1.5 m in girth. The bark is reddish brown,thin and scaly. The leaves are distichous and linear with recurved margin. Due to pointed apex they are called as needles. The male and female flowers are produced by different trees.

The Himalayan yew has long been used as a medicinal plant (Chopra *et al.*, 1956; Bahoray *et al.*, 1979; Bhakuni *et al.*, 1969; Khanna *et al.*, 1969; and Vohora *et al.*, 1971). Its leaves and fruits are credited with emmenagogue, anticephalalgic, sedative and antispasmodic properties. The leaves are used for the treatment of hysteria, epilepsy and nervousness. They are stomachic, antiasthmatic, cardiotonic and abortifacient. Aerial parts of the plant exhibit hypothermic activity.

Chemical investigation on the Himalayan yew has resulted in the isolation of its various chemical constituents (Table 1). The most important constituent is taxol (**1**) (Wanie *et al.*, 1971), a lead anticancer agent. Different other constituents also exhibit interesting biological properties. Here, we review briefly the chemsitry and bioactivity

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Table 1. Compounds Reported from the Himalayan Yew

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
A	TAXOIDS		
1	Taxol (**1**) $C_{47}H_{51}NO_{14}$ 198-203° (aq. MeOH) -42.0° (c 0.37, MeOH)	Needles, stems and roots, cultured cells and endophytic fungus, *Pestalotiopsis microspora*	Powell *et al.*, 1979; Miller *et al.*, 1981; George *et al.*, 1993; Velde *et al.*, 1994; Chattopadhyay *et al.*, 1994; Bashyal *et al.*, 1994; Zhang *et al.*, 1995a; Das, 1996a; Strobel *et al.*, 1996; Conneely *et al.*, 1996; Wang, 1997; Wang *et al.*, 1997; Singh *et al.*, 1997; Das *et al.*, 1998a, 1998b.
2	Cephalomannine (**2**) $C_{45}H_{53}NO_{14}$ 184-185° (aq. MeOH) -41.0° (c 0.39, MeOH)	Needles, stems and roots	Powell *et al.*, 1979; Miller *et al.*, 1981; Velde *et al.*, 1994; Zhang *et al.*, 1995a; Wang, 1997; Singh *et al.*, 1997.
3	Baccatin III (**3**) $C_{31}H_{38}O_{11}$ 229-231° ($CHCl_3$) -54.0° (c 0.41, MeOH)	Needles, stems and roots	Powell *et al.*, 1979; Miller *et al.*, 1981; Wang, 1997.
4	1-β-Hydroxybaccatin I (**4**) $C_{32}H_{44}O_{14}$ 237-238° (AcOMe-n-C_6H_{14}) +98.0° (c 1.01, $CHCl_3$)	Needles, stems and roots	Miller *et al.*, 1981; Barboni *et al.*, 1993; Chattopadhyay *et al.*, 1996a; Rojatkar *et al.*, 1996.
5	19-Hydroxybaccatin III (**5**) $C_{31}H_{37}O_{12}$ 171-172° (MeOH) -	Needles, stems and roots	McLaughlin *et al.*, 1981
6	10-Deacetyltaxol (**6**) $C_{41}H_{53}NO_{13}$ Amorphous -	Needles, stems and roots	McLaughlin *et al.*, 1981; Wang, 1997.
7	10-Deacetylcephalomannine (**7**) $C_{43}H_{51}NO_{13}$ Amorphous -	Needles, stems and roots	McLaughlin *et al.*, 1981.
8	10-Deacetylbaccatin III (**8**) $C_{29}H_{36}O_{10}$ 230-232° ($CHCl_3$) -	Needles and twigs	Appendin *et al.*, 1992; Barboni *et al.*, 1993; George *et al.*, 1993; Chattopadhyay *et al.*, 1994; Velde *et al.*, 1994; Das *et al.*, 1995b, 1995c, 1996e, 1998b, 1998c; Zhang *et al.*, 1995a; Das 1996a; Lee *et al.*, 1996; Reddy and Krupadanam, 1996; Rojatkar *et al.*, 1997; Singh *et al.*, 1997, Wang, 1997.
9	14β-Hydroxy-10-deacetylbaccatin III (**9**) $C_{29}H_{36}O_{11}$ 215-217° (MeOH) -43.2° (c 0.2, MeOH)	Needles	Appendino *et al.*, 1992; Das *et al.*, 1995c, 1996c; Das, 1996a
10	Brevifoliol (**10**) $C_{31}H_{40}O_9$ 200-202° (n-C_6H_{14}-Me_2CO) -24.0° (c 3.49, $CHCl_3$)	Needles and twigs	Barboni *et al.*, 1993; Appendino *et al.*, 1993a; George *et al.*, 1993; Velde *et al.*, 1994; Das *et al.*, 1995b, 1995c, 1996c, 1998b, 1998c; Chattopadhyay and Sharma, 1995b; Das, 1996a; Chattopadhyay *et al.*, 1996a

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
11	2-Debenzoyl-14β-benzoyloxy-10-deacetylbaccatin III (**11**) $C_{29}H_{36}O_{11}$ 160° (Me_2CO-Et_2O) -30.0° (c 0.37, MeOH)	Needles	Appendino *et al.*, 1993b
12	10,15-Epoxy-11-(15→1)-abeo-10-deacetylbaccatin III (**12**) $C_{29}H_{34}O_9$ Oil -18.0° (c 1.2, CH_2Cl_2)	Needles	Appendino *et al.*, 1993b
13	13-Decinnamoyltaxchinin B (Taxayuntin) (**13**) $C_{35}H_{44}O_{13}$ 227-228° (Me_2CO-n-C_6H_{14}) -40.0° (c 0.4825, MeOH)	Needles and Twigs	Barboni *et al.*, 1993; Appendino *et al.*, 1993a; Zhang *et al.*, 1994, 1995a; Das *et al.*, 1995a, 1995b, 1995c, 1996c, 1998b; Das, 1996a
14	13-Acetylbrevifoliol (**14**) $C_{33}H_{42}O_{10}$ Amorphous +8.0° (c 1.0, MeOH)	Needles	Barboni *et al.*, 1993; Appendino *et al.*, 1993a; Chattopadhyay *et al.*, 1996a
15	* (**15**) $C_{28}H_{40}O_{10}$ 232-233° (AcOMe-n-C_6H_{14}) +82.0° (c 1.01, MeOH)	Needles	Barboni *et al.*, 1993; Appendino *et al.*, 1993a.
16	* (**16**) $C_{22}H_{34}O_6$ 160-162° (AcOMe-n-C_6H_{14}) -24.0° (c 1.1, MeOH)	Needles	Barboni *et al.*, 1993; Appendino *et al.*, 1993a.
17	*(**17**) $C_{24}H_{36}O_8$ - -5.0° (c 0.95, MeOH)	Needles	Barboni *et al.*, 1993; Appendino *et al.*, 1993a.
18	2α-Acetoxybrevifoliol (Taxchinin A) (**18**) $C_{33}H_{42}O_{11}$ Amorphous -	Needles	Velde *et al.*, 1994; Chattopadhyay *et al.*, 1995b, 1996a.
19	Wallifoliol (**19**) $C_{29}H_{34}O_{10}$ Amorphous -10.8° (c 0.65, MeOH)	Needles	Velde *et al.*, 1994.
20	7,2'-Bisdeacetoxy austrospicatine (**20**) $C_{37}H_{51}NO_8$ 199-200° (Me_2CO) +112.9° (c 0.95, $CHCl_3$)	Stem bark	Zhang *et al.*, 1994, 1995a.
21	Taxacustin (10,13-Deacetylabeobaccatin IV (**21**) $C_{28}H_{40}O_{12}$ 220-222° -34.0° (c 1.0, MeOH)	Needles and stem bark	Zhang *et al.*, 1994, 1995a; Chattopadhyay *et al.*, 1995a

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
22	2-Deacetoxy-5-decinnamoyltaxinine J (**22**) $C_{28}H_{40}O_9$ 188-190° +114.0° (c 1.0, MeOH)	Stem bark	Zhang *et al.*, 1994, 1995a; Chattopadhyay *et al.*, 1995b.
23	2-Deacetoxytaxinine J (**23**) $C_{37}H_{46}O_{10}$ 162-164° (Me_2CO-n-C_6H_{14}) +77.7° (c 2.06, $CHCl_3$)	Stem bark and cultured cells	Zhang *et al.*, 1994, 1995a; Chattopadhyay *et al.*, 1995b, 1996a; Banerjee *et al.*, 1996; Rojatkar *et al.*, 1996; Das *et al.*, 1998b.
24	2'-Deacetoxy austrospicatine (**24**) $C_{39}H_{53}NO_{10}$ 158-160° (Me_2CO) +94.3° (c 0.705, $CHCl_3$)	Needles, stem bark and cultured cells	Zhang *et al.*, 1994, 1995a; Chattopadhyay *et al.*, 1996b; Banerjee *et al.*, 1996; Rojatkar *et al.*, 1997.
25	19-Debenzoyl-19-acetyltaxinine M (**25**) $C_{30}H_{40}O_4$ Gum +2.8° (c 0.35, $CHCl_3$)	Needles	Barboni *et al.*, 1995.
26	5-Cinnamoylbrevifoliol (Taxawallin C) (**26**) $C_{40}H_{46}O_{10}$ Oil -41.5° (c 0.91, $CHCl_3$)	Needles	Barboni *et al.*, 1995; Zhang *et al.*, 1995c.
27	10-Debenzoyl-2α-acetoxybrevifoliol (**27**) $C_{26}H_{36}O_{10}$ 180° +32.6° (c 2.2, MeOH)	Needles	Barboni *et al.*, 1995
28	7-Xylosyltaxol (**28**) $C_{52}H_{59}NO_{18}$ - -	Stem bark	Zhang *et al.*, 1995a.
29	10-Deacetyl-7-xylosyltaxol (**29**) $C_{50}H_{57}NO_{17}$ - -	Stem bark	Zhang *et al.*, 1995a.
30	10-Deacetyl-7-xylosyltaxol C (**30**) $C_{49}H_{63}NO_{18}$ - -	Stem bark and heart wood	Zhang *et al.*, 1995a; Chattopadhyay *et al.*, 1996e, 1997.
31	1-Hydroxy-2-deacetoxytaxinine J (Taxawallin A) (**31**) $C_{37}H_{46}O_{11}$ 112-114° +64.0° (c 0.58, $CHCl_3$)	Stem bark	Zhang *et al.*, 1995a, 1995b.
32	13-Acetyl-13-decinnamoyltaxchinin B (**32**) $C_{37}H_{46}O_{14}$ 243-244° (Me_2CO-n-C_6H_{14}) -54.0° (c 0.3219, $CHCl_3$)	Needles	Das *et al.*, 1995a

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
33	Taxawallin D (**33**) $C_{33}H_{42}O_{10}$ 122-124° -	Needles	Zhang *et al.*, 1995c.
34	Taxawallin F (**34**) $C_{26}H_{38}O_9$ 124-125° -	Needles	Zhang *et al.*, 1995c.
35	Taxawallin G (**35**) $C_{26}H_{38}O_9$ 270° (d) -	Needles	Zhang *et al.*, 1995b.
36	Taxawallin H (**36**) $C_{26}H_{38}O_9$ 72-74° -	Needles	Zhang *et al.*, 1995c.
37	13-Decinnamoyl-9-deacetyltaxchinin B (**37**) $C_{33}H_{42}O_{12}$ Amorphous -	Stem bark	Chattopadhyay *et al.*, 1996c.
38	*Dihydrotaxol* (**38**) $C_{47}H_{53}NO_{14}$ Amorphous -	*Stem bark*	Chattopadhyay *et al.*, 1996d.
39	9-O-Benzoyl-9,10-dideacetyl-11 (15→1)- abeobaccatin VI (**39**) $C_{40}H_{46}O_{13}$ Amorphous -88.0° (c 0.5, $CHCl_3$)	Stem bark and heart wood	Chattopadhyay *et al.*, 1996d, 1996e, 1997
40	9-O-Benzoyl-9-deacetyl-11 (15→1)-abeobaccatin VI (**40**) $C_{42}H_{48}O_{14}$ Amorphous -72.00 (c 0.5, $CHCl_3$)	Stem bark	Chattopadhyay *et al.*, 1996d
41	Taxusin (**41**) $C_{28}H_{40}O_8$ 125-126° -	Heart wood	Chattopadhyay *et al.*, 1996e, 1997
42	2α,5α,10β-Triacetoxy-14β-(2'-methyl)-butyryloxy-4 (20) 11-taxadine (**42**) $C_{31}H_{46}O_8$ 107-108° -	Heart wood	Chattopadhyay *et al.*, 1996e, 1997
43	Baccatin IV (**43**) $C_{32}H_{44}O_{14}$ 198-199° (Me_2CO-n-C_6H_{14}) -	Needles and stem bark	Chattopadhyay *et al.*, 1996a; Rojatkar *et al.*, 1996.

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
44	10-Deacetyl-7-epitaxol (**44**) $C_{45}H_{49}NO_{13}$ - -	Stems	Wang, 1997.
45	5-Deacetyl-1-hydroxybaccatin I (**45**) $C_{30}H_{42}O_{13}$ 208-210° (MeOAc-n-C_6H_{14}) +76.0° (c 1.0, EtOAc)	Needles	Barboni *et al.*, 1997
46	2-Dacetoxytaxinine B (**46**) $C_{35}H_{42}O_9$ 240° (d) (EtOAc-n-C_6H_{14}) +71.7° (c 0.03, $CHCl_3$)	Needles	Shrestha *et al.*, 1997.
B	PHENOLIC COMPOUNDS AND THEIR DERIVATIVES		
i)	Lignans		
47	(−)-secoisolariciresinol (**47**) $C_{20}H_{26}O_6$ 115-117° ($CHCl_3$-MeOH) -32.4° (c 0.4388, Me_2CO)	Needles, twigs and heart wood	Mujumdar *et al.*, 1972; Das *et al.*, 1993a, 1993b, 1994a, 1995b; Chattopadhyay *et al.*, 1997
48	Taxiresinol (**48**) $C_{19}H_{22}O_6$ 158° (Me_2CO) +32.2° (EtOH)	Needles and heart wood	Mujumdar *et al.*, 1972; Chattopadhyay *et al.*, 1997
49	Isotaxiresinol (**49**) $C_{19}H_{22}O_6$ 168-169° (aq. HOAc) -	Needles and heart wood	Mujumdar *et al.*, 1972; Das *et al.*, 1993a, 1993b, 1994a; Chattopadhyay *et al.*, 1997
50	Epimers of conidendrin (**50**) $C_{20}H_{20}O_6$ 230-237° (EtOH) -57.9° (c 0.14, Me_2CO)	Needles, stems and roots	Miller *et al.*, 1982; Das *et al.*, 1995d
51	Hydroxymatairesinol (**51**) $C_{20}H_{22}O_7$ Amorphous -0.95° (c 1.27, EtOH)	Needles, stems and roots	Miller *et al.*, 1982
52	Isoliovil (**52**) $C_{20}H_{24}O_7$ 170-172° (MeOH) -17.9° (c 0.22, EtOH)	Needles, stems and roots	Miller *et al.*, 1982
53	3-Demethyl-(−)-secoisolariciresinol (**53**) $C_{19}H_{24}O_6$ 125-126° ($CHCl_3$-MeOH) -29.7° (c 0.6476, MeOH)	Needles	Das *et al.*, 1993a, 1993b, 1994a
54	(+)-Isolariciresinol (**54**) $C_{20}H_{24}O_6$ 152-154° ($CHCl_3$-MeOH) +45.8° (c 0.5672, MeOH)	Needles	Das *et al.*, 1993a, 1993b, 1994a

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
55	4-O-Methyl-3'-O-demethyl-(−)-secoisolariciresinol (**55**) $C_{20}H_{26}O_6$ 137-138° ($CHCl_3$-MeOH) -27.2° (c 0.4218, MeOH)	Needles	Das *et al.*, 1994a
56	Suchilactone (**56**) $C_{21}H_{20}O_6$ 131-132° (C_6H_6) -85.5° (c 0.3494, $CHCl_3$)	Twigs	Das *et al.*, 1994a, 1998b
57	4'-O-Demethylsuchilactone (**57**) $C_{20}H_{18}O_6$ Oil -38.3° (c 0.2371, $CHCl_3$)	Twigs	Das *et al.*, 1994a
58	Lignan diol (**58**) $C_{21}H_{24}O_6$ 120-121° (C_6H_6) -38.7° (c 0.4239, $CHCl_3$)	Twigs	Das *et al.*, 1994a
59	(−)-Matairesinol (**59**) $C_{20}H_{22}O_6$ - -	Twigs and needles	Das *et al.*, 1995d
60	(−)-Hibalactone (**60**) $C_{20}H_{16}O_6$ - -	Twigs and needles	Das *et al.*, 1995d, 1998b
61	(−)-Isohibalactone (**61**) $C_{20}H_{16}O_6$ - -	Twigs and needles	Das *et al.*, 1995d
62	(−)-2-(3,4-Methylene-dioxybenzyl)-3(3,4-methylenedioxybenzylidene)-butane-1,4-diol (**62**) $C_{20}H_{20}O_6$ - -	Twigs and needles	Das *et al.*, 1995d
63	(−)-2-(3,4-Methylene-dioxybenzyl)-3-(3,4-dimethoxybenzylidene)-butane-1,4-diol (**63**) $C_{21}H_{24}O_6$ - -	Twigs and needles	Das *et al.*, 1995d
ii)	Biflavones		
64	Sciadopitysin (**64**) $C_{33}H_{24}O_{10}$ 315° (C_5H_5N-MeOH) -	Needles and branches	Khan *et al.*, 1976; Parveen *et al.*, 1985; Qiu *et al.*, 1989; Das *et al.*, 1995b; Reddy and Krupadanam, 1996; Shrestha *et al.*, 1997

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
65	Sequoiaflavone (**65**) $C_{31}H_{20}O_{10}$ 320° (C_5H_5N-MeOH) -.	Needles and branches	Khan *et al.*, 1976; Qiu *et al.*, 1989
66	Ginkgetin (**66**) $C_{32}H_{22}O_{10}$ 320° (C_5H_5N-MeOH) -	Needles and branches	Khan *et al.*, 1976; Qiu *et al.*, 1989; Das *et al.*, 1995b; Reddy and Krupadanam, 1996; Singh *et al.*, 1997
67	Amentoflavone (**67**) $C_{30}H_{18}O_{10}$ - -	Needles	Parveen *et al.*, 1985; Das *et al.*, 1994b
68	Kayaflavone (**68**) $C_{33}H_{24}O_{10}$ - -	Needles and twigs	Das *et al.*, 1994b, 1995b; Singh *et al.*, 1997
69	4',7"-Di-O-methyl-amentoflavone (**69**) $C_{32}H_{22}O_{10}$ - -	Needles	Das *et al.*, 1994b
70	7,4',7"-Tri-O-methyl-amentofalvone (**70**) $C_{33}H_{24}O_{10}$ - -	Needles	Das *et al.*, 1994b
iii)	Simple phenolics and their derivatives		
71	Betuloside [(-)-Rhododendrin] (**71**) $C_{16}H_{24}O_8$ 187-190° (EtOAc) -48.0° (c 1.0, H_2O)	Needles and twigs	Khan *et al.*, 1976; Das *et al.*, 1993b, 1994a, 1995b, 1998b
72	4-(4'-Hydroxyphenyl)-2R-butanol [(-)-Rhododendrol, (-)-Betuligenol] (**72**) $C_{10}H_{14}O_2$ - -17.8° (c 0.3151, EtOH)	Needles and twigs	Das *et al.*, 1993 a, 1993b, 1994a, 1995b, 1998b; Chattopadhyay *et al.*, 1994
73	4-(3',4'-Dihydroxyphenyl)-2R-butanol (**73**) $C_{10}H_{14}O_3$ - -18.1° (c 0.1245, EtOH)	Needles	Das *et al.*, 1993a, 1993b, 1994a
74	4-(3'-Methoxy-4'-hydroxyphenyl)-2R-butanol (**74**) $C_{11}H_{16}O_3$ - -16.3° (c 0.2572, EtOH)	Needles	Das *et al.*, 1993a, 1993b, 1994a

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
75	Arylpropanols (**75-77**) $C_9H_{12}O_2$, $C_9H_{12}O_3$ and $C_{10}H_{14}O_3$ - -	Needles	Das *et al.*, 1993b, 1994a
76	Taxuside (**78**) $C_{16}H_{20}O_9$ Amorphous -41.7° (c 0.2318, $CHCl_3$)	Needles	Das *et al.*, 1993b
77	p-Hydroxybenzaldehyde (**79**) $C_7H_6O_2$ 116-117° -	Needles	Chattopadhyay *et al.*, 1994; Das *et al.*, 1998b
78	4-(4'-Hydroxyphenyl)-2S-butanol (**80**) $C_{10}H_{14}O_2$ Viscous oil +21.5° (c 0.348, $CHCl_3$)	Needles	Rojatkar *et al.*, 1995
79	Methyl-β-orcinolcarboxylate (Atraric acid) (**81**) $C_{10}H_{12}O_4$ - -	Needles and twigs	Shrestha *et al.*, 1997
80	4-(4'-Hydroxyphenyl)-butan-2-one (**82**) $C_{10}H_{12}O_2$ - -	Needles	Das *et al.*, 1998b
81	4-(4'-Hydroxyphenyl)-*trans*-but-3-ene-2-one (**83**) $C_{10}H_{10}O_2$ - -	Needles	Das *et al.*, 1998b
iv)	Miscellaneous		
a)	Steroid		
82	β-sitosterol (**84**) $C_{29}H_{50}O$ - -	Heart wood	Mujimdar *et al.*, 1972; Zhang *et al.*, 1995a; Shrestha *et al.*, 1997
b)	Apocarotenoids		
83	Deglycosylicariside B_4 (**85**) $C_{13}H_{22}O_3$ Gum -102.0° ($CHCl_3$)	Needles	Appendino *et al.*, 1993c
84	12-Dehydro-deglycosylicariside B_4 (**86**) $C_{13}H_{20}O_3$ Oil -9.0° ($CHCl_3$)	Needles	Appendino *et al.*, 1993c

Table 1. Continued

S.No	Name (Structure) Mol. Formula m.p. (Solvent) $[\alpha]_D$ (Solvent)	Plant part (s) from which the compound was reported.	Reference
85	Vomifoliol (**87**) $C_{13}H_{20}O_3$ - -	Needles	Appendino *et al.*, 1993a
86	Dehydrovomifoliol (**88**) $C_{13}H_{18}O_2$ - -	Needles	Appendino *et al.*, 1993a
c)	Amino acid		
87	N-Benzoyl-(2R, 3S)-3-phenylisoserine (**89**) $C_{15}H_{15}NO_{14}$ 177-178° (EtOAc) -36.3° (c 0.7256, EtOH)	Needles	Das *et al.*, 1998c

† The compounds have been listed according to the chronological order of the first isolation from the Himalayan yew.

*The compounds whose names were not given in the original literature or whose names have been proved to be incorrect after revision of their structures are indicated only by their structure numbers

of the reported constituents of the plant.

Chemistry

The Himalayan yew has been chemically investigated extensively in recent years and a large number of compounds have been isolated and characterized from different parts of the plant (Table 1). These compounds are mainly taxoids and phenolics. The plant materials were generally extracted with methanol, ethanol or a mixture of methylene chloride (or chloroform) and methanol. The constituents were purified by different chromatographic techniques including column chromatography, preparative thin layer chromatography, countercurrent distribution and HPLC methods. The isolated compounds were identified from spectral and chemical evidences. The structures of the taxoids were established mainly by 1 D and 2D-NMR and FAB mass spectroscopic studies and by X-ray crystallographic analysis (Appendino, 1995; Madhusudanan *et al.*, 1997).

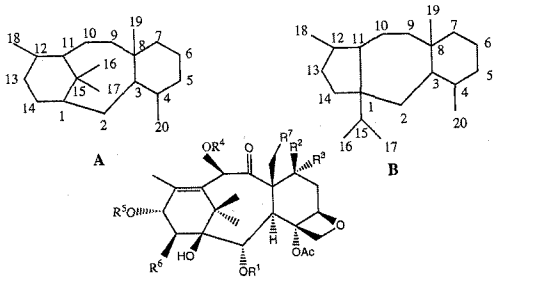
The taxoids isolated from the Himalayan yew have been observed with normal taxane skeleton or rearranged skeleton (Das *et al.*, 1995c, 1995e, 1996b). The normal taxoids contain 6/8/6-membered ring system (**A**) and the rearranged taxoids contain 5/7/6-membered ring system (**B**). The taxoids with B ring system are also known as 11 (15 → 1)- abeotaxoids (Appendino *et al.*, 1993a) or A-nortaxoids (Chen and Kingston, 1994). Among the normal taxoids, taxol (**1**) is the most important for its complex chemical structure and interesting anticaner activity. The compound was isolated from the Himalayan yew at first by Powell *et al.*, but initially they misidentified the species as *Cephalotaxus manni* (Powell *et al.*, 1979). The yield of taxol (**1**) was reported to be 0.001% from the ethanolic extract of the needles, stems and roots of the plant. George *et al.* reinvestigated the taxol content of the plant and they found the encouraging results; the concentration of taxol in some collections of needles ranged from 0.045-0.13% (George *et al.*, 1993). As

the needles are bioregenerable parts of the plant, the Himalayan yew may be considered as a valuable source of taxol. Different other workers have also reported the compound from the plant (Table 1). Recently the compound has been isolated from the cell culture of the yew (Wang, 1994; Conneely *et al.*, 1996 and Hong *et al.*, 1996) and also from the endophytic fungus, *Pestalotiopsis microspora* (Strobel *et al.*, 1996).

The Himalayan yew is also an important source of different other taxol-like diterpenoids, as for example, cephalomannine (**2**), 10-deacetyltaxol (**6**), 10-deacetylcephalomannine (**7**), dihydrotaxol (**38**) and 10-deacetyl-7-epitaxol (**44**) (references in Table 1). Some taxol analogues with β-xylosyl moiety at C-7 (e.g., compounds **28-30**) have also been reported. Two important precursors of taxol, baccatin III (**3**) and 10-deacetylbaccatin III (**8**) have been isolated. These two compounds can be utilised for the semisynthetic preparation of taxol (**1**). Taxol C-13 side chain [N-benzoyl-(2R,3S)-3-phenylisoserine (**89**)] has been isolated (Das *et al.*, 1998c) for the first time from the needles of the plant.

Several reactions of taxol (**1**) and taxol-like diterpenoids have been carried out. The acid-catalysed decomposition of taxol afforded baccatin III and 10-dacetylbaccatin III (Das *et al.*, 1998b). The olefinic double bound of the side chain of cephalomannine (**2**) was hydroxylated with osmium tetroxide under catalytic conditions (Kingston *et al.*, 1990 and Das *et al.*, 1996d). 10-Deacetyltaxol (**6**) and 10-deacetylcephalomannine (**7**) were found to be labile in aqueous methanol, each forming an equilibrium mixture with the C-7 epimer (Miller *et al.*, 1981).

Among the rearranged taxoids brevifoliol



1 R^1=Bz, R^2=OH, R^3=R^6=R^7=H, R^4=Ac, R^5=A

2 R^1=Bz, R^2=OH, R^3=R^6=R^7=H, R^4=Ac, R^5=B

3 R^1=Bz, R^2=OH, R^3=R^5=R^6=R^7=H, R^4=Ac,

5 R^1=Bz, R^2=R^7=OH, R^3=R^5=R^6=H, R^4=Ac,

6 R^1=Bz, R^2=OH, R^3=R^4=R^6=R^7=H, R^5=A

7 R^1=Bz, R^2=OH, R^3=R^4= R^6=R^7=H, R^5=B

8 R^1=Bz, R^2=R^6=OH, R^3=R^4=R^5=R^7=H

9 R^1=Bz, R^2=OH, R^3=R^4=R^5=R^6=R^7=H

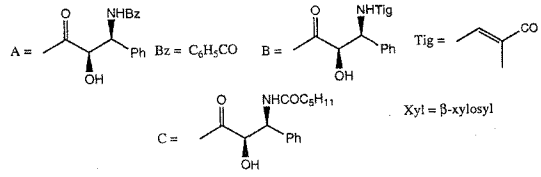
11 R^1= R^3=R^4=R^5=R^7=H, R^2=OH, R^6=OBz

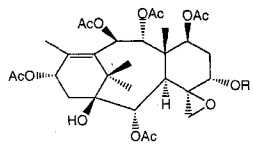
27 R^1=Bz, R^2=OXyl, R^3=R^6=R^7=H, R^4=Ac, R^5=A

28 R^1=Bz, R^2=OXyl, R^3=R^4=R^6= R^7=H, R^5=A

29 R^1=Bz, R^2=OXyl, R^3=R^4=R^6= R^7=H, R^5=C

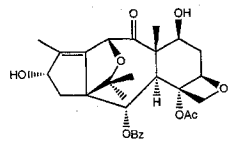
44 R^1=Bz, R^2=R^4=R^6=R^7=H, R^3=OH, R^5=A





4 R = Ac

45 R = H



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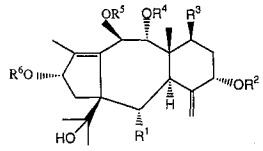


10 R^1=R^2=R^6=H, R^3=OAc, R^4=Ac, R^5=Bz

14 R^1=R^2=H, R^3=OAc, R^4=R^6=Ac, R^5=Bz

16 R^1=R^2=R^3=R^6=H, R^4=Ac, R^5=Bz

17 R^1=R^2=R^5=R^6=H, R^3=OAc, R^4=Ac

18 R^1=R^3=OAc, R^2=R^6=H, R^4=Ac, R^5=Bz

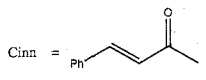
22 R^1=R^6=H, R^2=Cinn, R^3=OAc, R^4=Ac, R^5=Bz

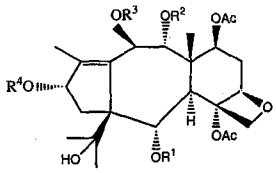
23 R^1=R^3=OAc, R^2=R^5=R^6=H, R^4=Ac

33 R^1=R^2=H, R^3=OAc, R^4=Bz, R^5=R^6=Ac

34 R^1=R^2=R^5=H, R^3=OAc, R^4=R^6=Ac

36 R^1=R^2= R^6=H, R^3=OAc, R^4=R^5=Ac





13 R^1=R^2=Ac, R^3=Bz, R^4=H

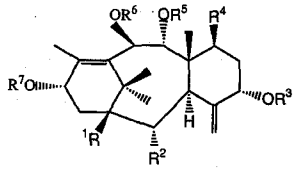
24 R^1=R^2=Ac, R^3=R^4=H

32 R^1=R^2=R^4=Ac, R^3=Bz

37 R^1=Ac, R^2=R^4=H, R^3=Bz

39 R^1=R^2=Bz, R^3=H, R^4=Ac

40 R^1=R^2=Bz, R^3=R^4=Ac



15 R^1=OH, R^2=R^3=H, R^4=OAc, R^5=R^6=R^7=Ac

20 R^1=R^2=R^4=H, R^3=$COCH_2CH(NMe_2)Ph$, R^5=R^6=R^7=Ac

25 R^1=R^2=R^3=H, R^4=OAc, R^5=R^6=R^7=Ac

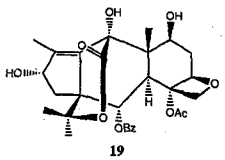
26 R^1=R^2=H, R^3=Cinn, R^4=OAc, R^5=R^6=R^7=Ac

30 R^1=R^2=H, R^3=$COCH_2CH(NMe_2)Ph$, R^4=OAc, R^5=R^6=R^7=Ac

31 R^1=OH, R^2=H, R^3=Cinn, R^4=OAc, R^5=R^6=R^7=Ac

35 R^1=R^4=OH, R^2=R^5=H, R^3=R^6=R^7=Ac

41 R^1=R^2=H, R^3=R^5=R^6=R^7=Ac, R^4=H



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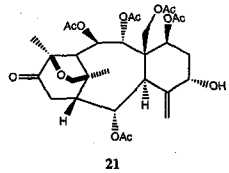

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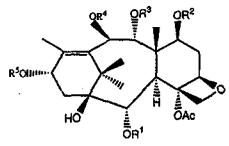
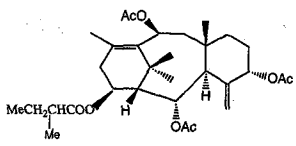


38 R^1=Bz, R^2=R^3=H, R^4=Ac, R^5=A

43 R^1=R^2=R^3=R^4=R^5=Ac



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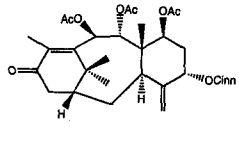

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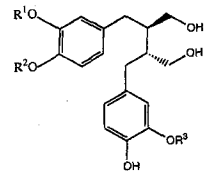
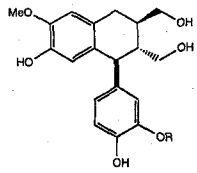


47 R^1=R^3=Me, R^2=H

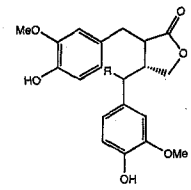
53 R^1=R^2=H, R^3=Me

55 R^1=R^2=Me, R^3=H



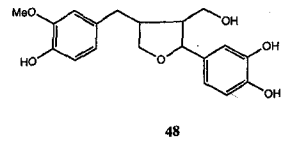
49 R=H

54 R=Me



51 R=OH

59 R=H



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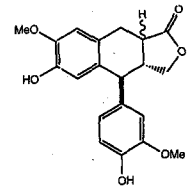

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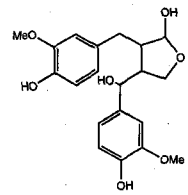

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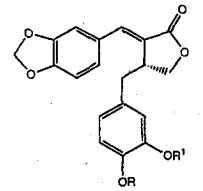
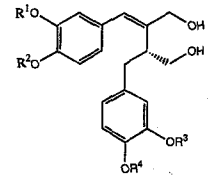


56 R=R^1=Me

57 R=H, R^1=Me

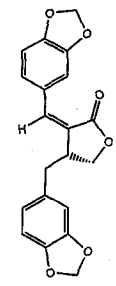
60 R,R^1=CH_2



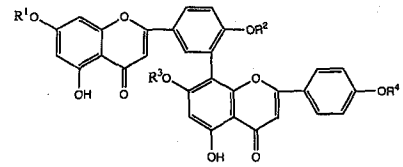
58 R^1,R^2=CH_2, R^3=R^4=Me

62 R^1,R^2=R^3,R^4=CH_2

63 R^1=R^2=Me, R^3,R^4=CH_2



61



64 R^1=R^2= R^4=Me,R^3=H

65 R^1=Me, R^2= R^3=R^4=H

66 R^1=R^2=Me, R^3=R^4=H

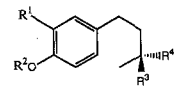
67 R^1=R^2=R^3=R^4=H

68 R^1=R^2=R^4=Me, R^3=H

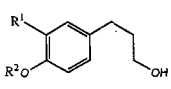
69 R^1=R^4=H, R^2=R^3=Me

70 R^1=R^2=R^3=Me, R^4=H

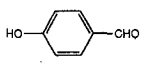
(10) is the most abundant. The compound was initially considered (Barboni *et al.*, 1993)



71 R^1=R^2=R^3=H, R^4=OGlc
72 R^1=R^2=R^3=H, R^4=OH
73 R^1=R^4=OH, R^2=R^3=H
74 R^1=OMe, R^2=R^3=H, R^4=OH
78 R^1=OH, R^2=R^3=H, R^4=OGlc
80 R^1=R^2=R^4=H, R^3=OH
82 R^1=R^2=H, R^3, R^4=O



75 R^1=R^2=H
76 R^1=OH, R^2=H
77 R^1=OMe, R^2=H



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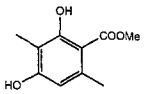

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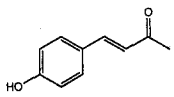
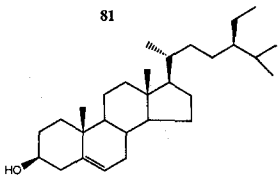


83



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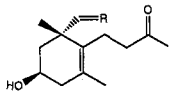
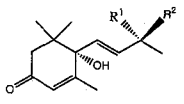
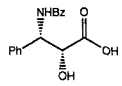


85 R=H, OH
86 R=O



87 R^1=OH, R^2=H
88 R^1, R^2=O



89

to be a normal taxoid but later its structure was correctly established (Appendino *et al.*, 1993) as an 11 (15 → 1)-abeotaxoid. Several analogues of brevifoliol have been reported from the Himalayan yew. Some other rearranged taxoids have been observed with an oxetane ring. These are mainly the derivatives of taxchinin B (Das *et al.*, 1995 a). One novel rearranged taxoid, wallifoliol (**19**) (Velde *et al.*, 1994) which contains a 5/6/6/6/4-membered ring system has been reported from the needles of the plant.

The phenolics are also the major constituents of the Himalayan yew. A large number of lignans, biflavones and simple phenolic compounds have been isolated. The lignans are mainly (−)-secoisolariciresinol and (+)-isolariciresinol derivatives. Some butyrolactone lignans (**51, 56, 57, 59-61**) have also been characterised. Semisynthesis and total synthesis of several lignans have been achieved (Das *et al.*, 1995 b; 1998 b).

The biflavonoids were also obtained in high concentration from the needles of the plant. All the compounds possess amentoflavone skeleton. However, no any new compound have so far been reported.

Several arylbutanols (**71-74, 78** and **80**) and arylpropanols (**75-77**) are the constitutents of the needles and twigs. The structures and the stereochemistry of the arylbutanols were settled by chemoenzymatic method (Das *et al.*, 1993a). (−)-Rhododendrol (**72**) and (−)-rhododendrin (**71**) are the major compounds in this group.

Among the other constituents apocarotenoids (**85-88**) (Appendino *et al.*, 1993c) are interesting. The Himalayan yew is the only yew species which can biogenetically produce such compounds.

Bioactivity

The taxoid constituents of the Himalayan yew are very important for their anticancer activity. Taxol (**1**) has been found (Wani *et al.*, 1971; Rowinsky *et al.*, 1990; Kingston *et al.*, 1990; Cragg *et al.*, 1993 and Das *et al.*, 1996) to be an exceptionally promising cancer chemotherapeutic agent with an unusually broad spectrum of potent antileukemic and tumour-inhibiting properties. The compound has shown excellent activity against drug-refractory human ovarian cancer and metastatic breast cancer (McGuire *et al.*, 1989 and Holmes *et al.*, 1991). The U.S Food and Drug Administration (FDA) has approved the compound for treatment of ovarian cancer and breast cancer in 1992 and 1994 respectively (Kingston, 1994 and Chen and Farina, 1995). Taxol belongs to a new series of antimitotic compounds having an unique mode of action on tubulin-microtubules system. It promotes tubulin polymerization and stabilizes microtubules against depolymerization (Schiff *et al.*, 1979, 1981; Parness *et al.*, 1981 and Manfredi *et al.*, 1984). However, toxicity and

lipophilicity of the compound are the disadvantages of making it as a drug (Vyas, 1996).

The KB and P-388 activities of cephalomannine (**2**) are roughly comparable to those of taxol (**1**) (Miller *et al.*, 1981). Both the compounds showed cytotoxicity against KB cell culture at 10^{-3}/g/ml. 10-Deacetyltaxol (**6**) and 10-deacetylcephalomannine (**7**) and their C-7 epimers also showed significant cytotoxic activity (McLaughlin *et al.*, 1981). The results indicated that the 10-acetyl group and the β-hydroxyl at C-7 are not essential to the cytotoxic effect of taxol and cephalomannine.

Baccatin III (**3**), 10-deacetylbaccatin III (**8**) and 1-β-hydroxybaccatin I (**4**) were found to be far less active than taxol (**1**) while 19-hydroxybaccatin III (**5**) was inactive. Thus it appears that the C-13 side chain and the oxetane ring of taxol are very important for its activity (Kingston, 1994).

Among the other taxoids isolated from the Himalayan yew dihydrotaxol (**38**) (Chattopadhyay *et al.*, 1996d) showed better activity than taxol. 2-Deacetoxytaxinine J (**23**) (Rojatkar *et al.*, 1996) increased cellular accumulation of vincristine (VCR) in multidrug resistant tumour cell while taxol did not exhibit such a property.

Some of the rearranged taxoids have also been tested for their activity but none of them showed promosing results. Brevifoliol (**10**) (Geroge *et al.*, 1993) has been evaluated to possess no activity in tubulin assays and showed modest cytotoxicity against KB cells.

The mixture of biflavonoids isolated from the Himalayan yew was tested on albino rats and mice and it showed CNS depressant, analgesic and antipyretic properties (Vohora *et al.*, 1980). (−)-Hibalactone (**60**) was found to possess insecticidal activity (Das *et al.*, 1998b). (−) and (+)-Rhododendrols (**72** and **80**) and (−)-rhododendrin (**71**) were proved to exhibit significant hepatoprotective effect (Shinoda, *et al.*, 1986; Parmar *et al.*, 1991 and Das *et al.*, 1998b). Thus the Himalayan yew may be considered as a potential source of different types of bioactive natural products.

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