

# *Plectranthus barbatus*: A Review of Phytochemistry, Ethnobotanical Uses and Pharmacology – Part 1

## Authors

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## Key words

- *Plectranthus barbatus*
- Lamiaceae
- forskolin
- phytochemistry
- ethnobotanical uses
- pharmacology
- 6-(3-dimethylaminopropionyl)forskolin hydrochloride (NKH477)

## Abstract

*Plectranthus barbatus* Andr. is one of the most important species of the genus *Plectranthus* L' Herit. (Lamiaceae), with a wide variety of traditional medicinal uses in Hindu and Ayurvedic traditional medicine as well as in the folk medicine of Brazil, tropical Africa and China. The plant has therefore been an attractive target for intensive chemical and pharmacological studies up to now. This review presents data about the phytochemistry, ethnobotanical uses and pharmacology of *Plectranthus barbatus* as well as the pharmacology of its constituents. In addition to essential oil, abietane diterpenoids and 8,13-epoxy-labd-14-en-11-one diterpenoids are the main constituents found in *Plectranthus barbatus*. The major ethnobotanical uses are for intestinal disturbance and

liver fatigue, respiratory disorders, heart diseases and certain nervous system disorders. Forskolin as one of the major constituents with its unique adenylyl cyclase activation that underlies the wide range of pharmacological properties could explain the different traditional uses of *Plectranthus barbatus*. Forskolin is involved in a number of patented pharmaceutical preparations used as over-the-counter drugs for the treatment of several ailments. However, the water-insoluble nature of forskolin limits its clinical usefulness. Forskolin thus served as a prototype for the development of 6-(3-dimethylaminopropionyl)forskolin hydrochloride (NKH477) as a potent water-soluble forskolin derivative that finds use in the therapy for a number of diseases especially of the cardiovascular system.

## Introduction

*Plectranthus* L' Herit., is a complex genus of the family Lamiaceae (Labiatae) that contains about 300 species distributed in tropical Africa, Asia and Australia [1]. Taxonomically the genera *Coleus* and *Plectranthus* are recombinated by the Japanese authors to the genus *Plectranthus* [2]. One of the most important species of this genus is *Plectranthus barbatus* Andr., which is commonly referred to by a number of synonyms such as *Plectranthus forskohlii* Briq., *Plectranthus forskalaei* Willd., *Plectranthus kilimandschari* (Gürke) H.L. Maass., *Plectranthus grandis* (Cramer) R.H. Willemse, *Coleus forskohlii* Briq., *Coleus kilimandschari* Gürke ex Engl., *Coleus coerulescens* Gürke, *Coleus comosus* A. Rich., and *Coleus barbatus* (Andr.) Benth [1]. *Plectranthus barbatus* grows perennially over the tropical and subtropical regions of the Indian subcontinent and is cultivated commercially for its use in pickles. It is also distributed over parts of Pakistan, Sri Lanka, tropical

East Africa, Asia (South of Arabian Peninsula, China) and Brazil [3–5].

*P. barbatus* is one of the most commonly used medicinal species of the genus *Plectranthus*. A diversity of traditional medicinal uses of *P. barbatus* in India (Hindu and Ayurvedic medicine), East and Central Africa, China, and Brazil have been reported. The majority of uses are for intestinal disturbance and liver fatigue, respiratory disorders, heart diseases and certain central nervous system disorders [1, 3, 4, 6, 7]. *P. barbatus* root extracts, such as the 50% ethanolic and methanolic extracts were therefore, in the middle of the 1970s, independently involved in screening programs for biological activities such as cardiovascular properties in the Central Drug Research Institute (CDRI), Lucknow, India, and by the group at Hoechst India Limited in Bombay, India. Reports from both research groups revealed the hypotensive and antispasmodic effects of the root extracts as well as the isolation of the major active principle which was named coleonol by CDRI [6, 8, 9],

received May 19, 2009  
 revised Dec. 7, 2009  
 accepted January 25, 2010

## Bibliography

DOI <http://dx.doi.org/10.1055/s-0029-1240898>  
 Published online February 22, 2010  
 Planta Med 2010; 76: 653–661  
 © Georg Thieme Verlag KG  
 Stuttgart · New York ·  
 ISSN 0032-0943

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**Table 1** Diterpenoids isolated from *Plectranthus barbatus*.

No. of the compound	Name of the compound	Part <sup>a</sup> used	<i>P. barbatus</i> location	References
<b>Abietane diterpenoids</b>				
1	(+)-Allylroleanone (plectranthone J)	L	East Africa – Kenya	[15]
2	Coleon S	L	China	[16, 17]
3	Coleon O	L	East Africa – Kenya	[18]
4	Coleon T	L	China	[16, 17]
5	Plectrin	L	East Africa – Kenya	[15, 18]
6	Barbatusin	L	Brazil	[7, 19, 20]
7	3 $\beta$ -Hydroxy-3-deoxybarbatusin	L	Brazil	[7]
8	Cyclobutatusin	L	Brazil	[7, 19, 21]
9	7 $\beta$ -Acetyl-12-deacetoxy-cyclobutatusin	L	Brazil	[19]
10	(16R)-Coleon E	L	East Africa – Kenya	[15, 22]
11	Coleon F	L	East Africa – Kenya	[15, 23]
12	(16R)-Plectrinon A	L	Brazil, East Africa – Kenya	[3, 15]
13	Plectrinon B	L	East Africa – Kenya	[15]
14	14-Deoxycoleon U	R	China	[24]
15	Coleon C	WP	China	[25]
16	6,7-Secoabietane diterpene I	S	Brazil	[26]
17	6,7-Secoabietane diterpene II	S	Brazil	[26]
18	Cariocal	S	Brazil	[27]
19	Abietatriene (dehydroabietane)	R	India	[28]
20	Demethylcryptojaponol (11-hydroxysugiol)	R	China	[24]
21	Ferruginol	S	Brazil	[29]
22	Sugiol	WP	China	[30]
23	20-Deoxocarnosol	S	Brazil	[31, 32]
24	6 $\beta$ -Hydroxycarnosol	S	Brazil	[33]
25	Barbatusol	S	Brazil	[29]
<b>8,13-Epoxy-labd-14-en-11-one-diterpenoids</b>				
26	Forskolin (7 $\beta$ -acetoxy-1 $\alpha$ ,6 $\beta$ ,9 $\alpha$ -trihydroxy-8,13-epoxy-labd-14-en-11-one; coleonol; colforsin; 1-deacetylforskolin B, 6-deacetylforskolin J)	R, R	India, China	[5, 10, 34–37]
27	9-Deoxyforskolin (7 $\beta$ -acetoxy-1 $\alpha$ ,6 $\beta$ -dihydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[5, 35, 38]
28	1,9-Dideoxyforskolin (7 $\beta$ -acetoxy-6 $\beta$ -hydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[5, 10, 35]
29	1,9 Dideoxy-7-deacetylforskolin (6 $\beta$ ,7 $\beta$ -dihydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[5, 10, 35]
30	Deacetyl-1-deoxyforskolin (6 $\beta$ ,7 $\beta$ ,9 $\alpha$ -trihydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[35]
31	6-Acetyl-1-deoxyforskolin	WP	China	[39]
32	6-Acetyl-1,9-dideoxyforskolin	WP	China	[39]
33	1,6-Di-O-acetylforskolin (1 $\alpha$ ,6 $\beta$ ,7 $\beta$ -tri-acetoxy-9 $\alpha$ -hydroxy-8,13-epoxy-labd-14-en-11-one; forskolin A; 1,7-diacetyl-forskolin)	R, WP	China	[4, 40, 41]
34	1-Acetylforskolin (1 $\alpha$ ,7 $\beta$ -diacetoxy-6 $\beta$ ,9 $\alpha$ -dihydroxy-8,13-epoxy-labd-14-en-11-one; forskolin B)	R, WP	China	[4, 40, 41]
35	Isoforskolin (6 $\beta$ -acetoxy-1 $\alpha$ ,7 $\beta$ ,9 $\alpha$ -trihydroxy-8,13-epoxy-labd-14-en-11-one; coleonol B; forskolin C; 1-deacetylforskolin I)	R, R, L, WP	India, China	[4, 10, 16, 37, 40–45]
36	1,9-Dideoxycoleonol B (7 $\beta$ -hydroxy-6 $\beta$ -acetoxy-8,13-epoxy-labd-14-en-11-one)	R	India,	[46]
37	7-Deacetylforskolin (1 $\alpha$ ,6 $\beta$ ,7 $\beta$ ,9 $\alpha$ -tetrahydroxy-8,13-epoxy-labd-14-en-11-one; deacetylforskolin; 6-deacetyl-forskolin; forskolin D)	R, R, WP	India, China	[4, 5, 10, 35, 40, 41]
38	Forskolin E (1 $\alpha$ ,7 $\beta$ -diacetoxy-6 $\beta$ -hydroxy-8,13-epoxy-labd-14-en-11-one; 9-dehydroxyforskolin B)	R, WP	China	[4, 47]
39	Forskolin F (7 $\beta$ -acetoxy-6 $\beta$ ,9 $\alpha$ -dihydroxy-8,13-epoxy-labd-14-en-11-one; 1-deoxyforskolin; 1-deacetoxyforskolin B; coleonol D)	R, R, WP	India, China	[4, 35, 43, 47, 48]
40	Forskolin G (1 $\alpha$ -hydroxy-6 $\beta$ ,7 $\beta$ -diacetoxy-8,13-epoxy-labd-14-en-11-one; 1-deacetyl-9-dehydroxyforskolin A; 1-deacetyl-6-acetylforskolin E)	R, WP	China	[44, 45, 47, 49, 50]
41	Forskolin H (1 $\alpha$ ,6 $\beta$ -diacetoxy-8,13-epoxy-labd-14-en-11-one; 7-deacetoxy-9-dehydroxyforskolin A; plectromatin C)	R, WP	China	[44, 45, 47, 49]
42	Forskolin I (1 $\alpha$ ,6 $\beta$ -diacetoxy-7 $\beta$ ,9 $\alpha$ -dihydroxy-8,13-epoxy-labd-14-en-11-one; 7-deacetylforskolin A; 1-acetylforskolin C)	R, WP	China	[44, 45, 51, 52]
43	Forskolin J (1 $\alpha$ ,9 $\alpha$ -dihydroxy-6 $\beta$ ,7 $\beta$ -diacetoxy-8,13-epoxy-labd-14-en-11-one; 6-O-acetylforskolin; 1-deacetylforskolin A; 7-acetylforskolin C)	R	China	[44, 51, 52]
44	1,6-Diacetoxy-9-deoxyforskolin (1 $\alpha$ ,6 $\beta$ ,7 $\beta$ -tri-acetoxy-8,13-epoxy-labd-14-en-11-one; forskolin K; 9-dehydroxyforskolin A)	R, WP	China	[30, 44, 52]
45	6 $\beta$ -Hydroxy-8,13-epoxy-labd-14-en-11-one (forskolin L)	R, R	China, India	[35, 44, 52] (continued)

Table 1 Continued

No. of the compound	Name of the compound	Part <sup>a</sup> used	<i>P. barbatus</i> location	References
46	Coleosol (6 $\beta$ ,9 $\beta$ -dihydroxy-8,13-epoxy-labd-14-en-11-one; 6 $\beta$ ,9 $\beta$ -dihydroxy-11-oxomanoyloxide)	R	India	[43, 53]
47	1-Acetoxy coleosol (1 $\alpha$ -acetoxy-6 $\beta$ ,9 $\alpha$ -dihydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[46]
48	Coleol (9 $\alpha$ -hydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[35, 43, 54, 55]
49	11-Oxomanoyloxide (8,13-epoxy-labd-14-en-11-one)	R	India	[35]
50	Coleonol E (7 $\alpha$ -acetoxy-6 $\beta$ -hydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[56]
51	Coleonol F (6 $\beta$ -acetoxy-7 $\alpha$ ,9 $\alpha$ -dihydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[56]
52	Deoxycoleonol (7 $\alpha$ -acetoxy-1 $\alpha$ ,6 $\beta$ -dihydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[57]
<b>8,13-Epoxy-labd-diterpenoids with some deviations</b>				
53	3-Hydroxyforskolin	WP	China	[58]
54	3-Hydroxyisoforskolin	WP	China	[58]
55	13-Epi-9-deoxycoleonol (13-epi-9-deoxyforskolin; 7 $\beta$ -acetoxy-1 $\alpha$ ,6 $\beta$ -dihydroxy-8,13-epoxy-labd-14-en-11-one)	R	India	[59]
56	Coleonol C (6 $\beta$ -acetoxy-1 $\alpha$ ,7 $\alpha$ ,9 $\alpha$ -trihydroxy-8,13- $\beta$ -epoxy-labd-14-en-11-one)	R	India	[57]
57	Coleonone (8,13-epoxy-labd-14-en-12-one)	R	India	[54, 55]
58	Manoyl oxide (8,13-epoxy-labd-14-ene)	R	India	[28]
<b>Miscellaneous labdane diterpenoids</b>				
59	13-Epi-sclareol	R	India	[60]
60	Forskoditerpene A (5 $\beta$ ,9 $\beta$ ,10 $\alpha$ ,12 $\beta$ -9,12-cyclo-7,13E-labdadien-15-oic acid)	WP	China	[61]
61	12-Hydroxy-8,13E-labdadien-15-oic acid	WP	China	[39]
62	Coleolic acid (11-ol,13-Me,8(9),13(14)Zlabdadien-15-oic acid)	WP	China	[62]
63	Coleonic acid (11-one,13-Me,8(9),13(14)Zlabdadien-15-oic acid)	WP	China	[62]
<b>8,13-Epoxy-labd-14-en-11-one-diterpene glycosides</b>				
64	Forskoditerpenoside A (6 $\beta$ -acetoxy-7 $\beta$ ,9 $\alpha$ -dihydroxy-8,13-epoxy-labd-14-en-11-one-1 $\alpha$ -O- $\beta$ -D-glucopyranoside)	WP	China	[63]
65	Forskoditerpenoside B (6 $\beta$ ,7 $\beta$ -diacetoxy-9 $\alpha$ -hydroxy-8,13-epoxy-labd-14-en-11-one-1 $\alpha$ -O- $\beta$ -D-glucopyranoside)	WP	China	[63]
66	Forskoditerpenoside C (6 $\beta$ -acetoxy-7 $\beta$ -hydroxy-8,13-epoxy-labd-14-en-11-one-1 $\alpha$ -O- $\beta$ -D-glucopyranoside)	WP	China	[61]
67	Forskoditerpenoside D (6 $\beta$ ,7 $\beta$ -diacetoxy-8,13-epoxy-labd-14-en-11-one-1 $\alpha$ -O- $\beta$ -D-glucopyranoside)	WP	China	[61]
68	Forskoditerpenoside E (6 $\beta$ -acetoxy-8,13-epoxy-labd-14-en-11-one-1 $\alpha$ -O- $\beta$ -D-glucopyranoside)	WP	China	[61]

<sup>a</sup> L = leaf; R = root; S = stem; WP = whole plant

and forskolin (**26**) (see **Fig. 2**) by Hoechst India Limited [5, 10]. Subsequent chemical analysis and NMR spectral studies revealed the identity of both compounds [11–13]. Additionally, a great number of constituents of *P. barbatus* were isolated and the pharmacology of some of them was unraveled.

The unique ability of forskolin (**26**) to stimulate adenylyl cyclase directly, not through  $\beta$ -adrenoreceptors, in different broken cell preparations as well as in intact tissues, with a consequently increasing level of adenosine 3',5'-cyclic monophosphate (cAMP) [5, 14], still motivates a great deal of scientific investigations of forskolin, forskolin derivatives and other constituents of *P. barbatus*. The biological profile, mechanism of action as well as the biochemical properties of forskolin have been revealed through a great number of studies worldwide. Although forskolin has been used in diverse studies for over 30 years, it will most likely continue to be an important tool to study the variety of cellular processes.

Due to the importance of *P. barbatus* in traditional medicine and as a source of forskolin, a general adenylyl cyclase activator with a great variety of pharmacological effects, the increasing use of the plant extracts standardized with certain amounts of forskolin as well as forskolin as over-the-counter drugs in spite of its clinical

uselessness because of its nonspecific general activation of adenylyl cyclase and low water solubility, and the distribution of information regarding *P. barbatus* under a number of synonymous Latin names, the purpose of this review is to provide data about the phytochemistry, ethnobotanical uses and pharmacology of *P. barbatus* and its major constituents such as forskolin (**26**) (see **Fig. 2**) and to delineate the potential of forskolin for the development of the novel water-soluble forskolin derivate, the 6-(3-dimethylaminopropionyl)forskolin hydrochloride (NKH477) (**79**) (see **Fig. 7**) as a substantial therapeutic agent.

### Phytochemistry



*P. barbatus*, especially that grown in India, Brazil, East Africa (Kenya) and China has been an attractive target for intensive chemical and pharmacological studies for novel biologically active constituents. The main constituents isolated from different parts of *P. barbatus* are diterpenoids and essential oil.

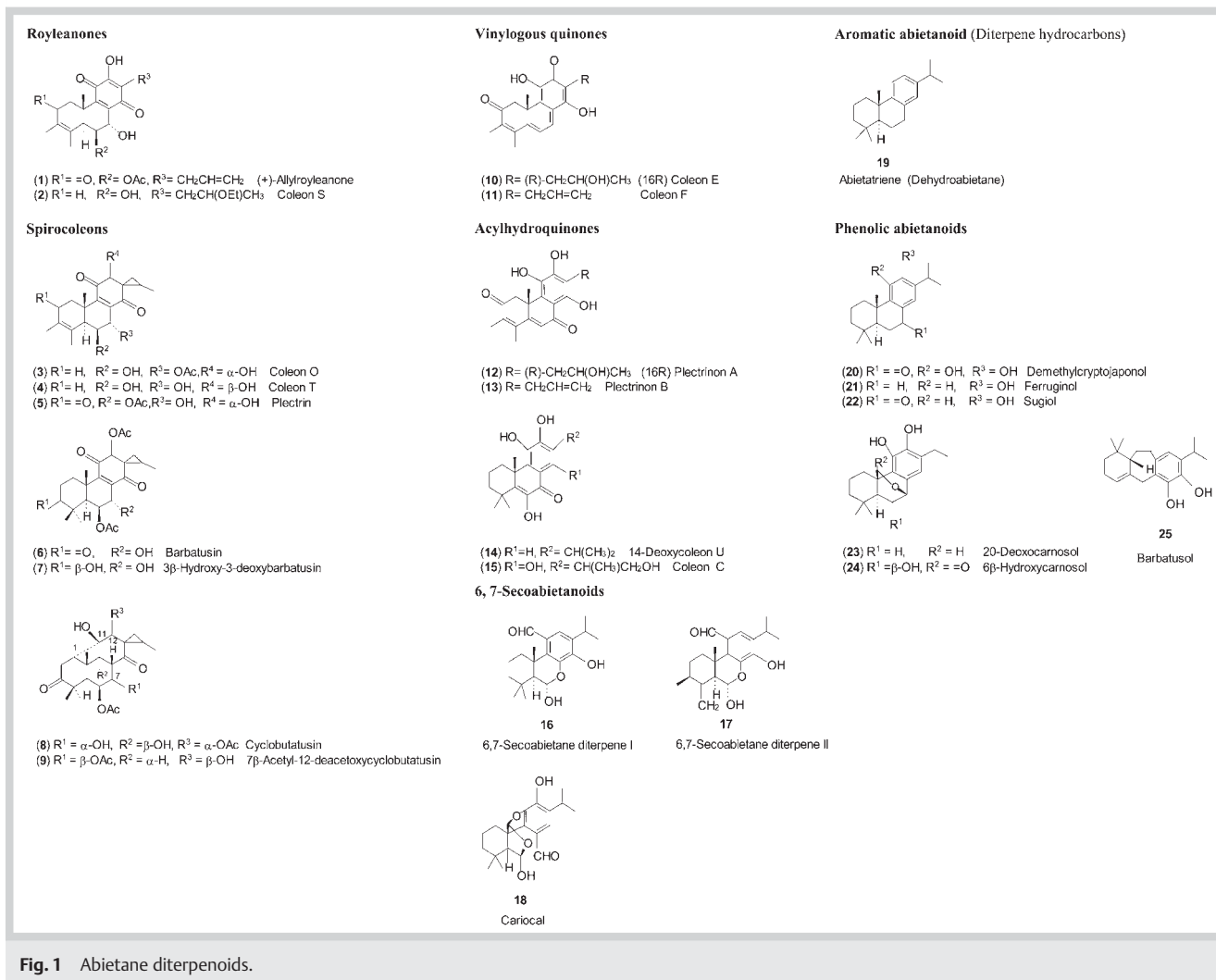
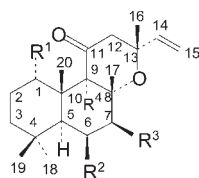


Fig. 1 Abietane diterpenoids.

## Diterpenoids

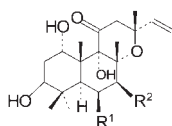
Two main groups of diterpenoids, the abietane diterpenoids (abietanoids) and the 8,13-epoxy-labd-14-en-11-one diterpenoids were identified in *P. barbatus*. Table 1 demonstrates the diterpenoids isolated from different parts of *P. barbatus*. Although the majority of abietane diterpenoids were isolated from the leaves and stems of *P. barbatus* growing in Brazil and from the leaves of *P. barbatus* distributed in East Africa (Kenya), some of them were also obtained from the leaves, roots and whole plant as well as from the roots of *P. barbatus* growing in China and India respectively (Table 1). The identified abietanoids are of various structures which could be classified accordingly into royleanones {(+)-allylroyleanone (1) [15] and coleon S (2) [16, 17]}, spirocoleons {coleon O (3) [18], coleon T (4) [16, 17], plectrin (5) [15, 18], barbalusin (6) [7, 19, 20], 3β-hydroxy-3-deoxybarbalusin (7) [7], cyclobutatusin (8) [7, 19, 21] and 7β-acetyl-12-deacetylcyclobutatusin (9) [19]}, vinylogous quinones (also named quinone methides) {(16R)-coleon E (10) [15, 22] and coleon F (11) [15, 23]}, acylhydroquinones {(16R)-plectrinon A (12) [3, 15], plectrinon B (13) [15], 14-deoxycoleon U (14) [24] and coleon C (15) [25]}, 6,7-secoabietanoids {6,7-secoabietane diterpene I (16), 6,7-secoabietane diterpene II (17) [26] and carioical (18) [27]}, aromatic abietanoids such as abietatriene (19) [28], phenolic abietanoids {demethylcryptojaponol (20) [24], fer-

ruginol (21) [29], sugiol (22) [30], 20-deoxocarnosol (23) [31, 32] and 6β-hydroxycarnosol (24) [33]}, including that with a rearranged abietane skeleton {barbalusol (25) [29]} (Fig. 1). A series of labdane diterpenoids with the typical 8,13-epoxy-labd-14-en-11-one skeleton, differentiated in the substituent groups at C-1, C-6, C-7, and C-9 (structures 26–52) (Fig. 2) were isolated mainly from the roots of *P. barbatus* grown in India as well as from the whole plant, roots, leaves of *P. barbatus* grown in China [4, 5, 10, 16, 30, 34–57] (Table 1). Forskolin (26) (Fig. 2) is the first main labdane diterpenoid isolated from the roots of the Indian *P. barbatus*. Some 8,13-epoxy-labdane diterpenoids with some deviations from the basic structure were identified, for example, those containing an additional hydroxy substituent at C-3 such as 3-hydroxyforskolin (53), and 3-hydroxyisoforskolin (54) [58], those with a β-axial orientation of the C-13/C-14 bond and α-equatorial orientation of the methyl group at C-16 such as 13-epi-9-deoxycoleonol (55) [59], and coleonol C (56) [57], or with the carbonyl function at C-12 or without carbonyl function such as coleonone (57) [54, 55], and manoyl oxide (58) [28] respectively (Table 1, Fig. 3). Further labdane diterpenoids such as 13-epi-sclareol (59) [60], forskoditerpene A (60) [61], 12-hydroxy-8,13E-labdadien-15-oic acid (61) [39], coleolic acid (62) and coleonic acid (63) [62] were also isolated from different parts of *P. barbatus* (Table 1, Fig. 4). Moreover, five mi-

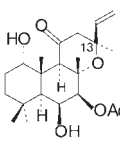


R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>	Compound
OH	OH	OAc	OH	Forskolin (26)
OH	OH	OAc	H	9-Deoxyforskolin (27)
H	OH	OAc	H	1,9-Dideoxyforskolin (28)
H	OH	OH	H	1,9-Dideoxy-7-deacetylforskolin (29)
H	OH	OH	OH	Deacetyl-1-deoxyforskolin (30)
H	OAc	OAc	OH	6-Acetyl-1-deoxyforskolin (31)
H	OAc	OAc	H	6-Acetyl-1,9-dideoxyforskolin (32)
OAc	OAc	OAc	OH	1,6-Di-O-acetylforskolin (forskolin A) (33)
OAc	OH	OAc	OH	1-Acetylforskolin (forskolin B) (34)
OH	OAc	OH	OH	Isoforskolin (coleonol B, forskolin C) (35)
H	OAc	OH	H	1,9-Dideoxycoleonol B (36)
OH	OH	OH	OH	7-Deacetylforskolin (forskolin D) (37)
OAc	OH	OAc	H	Forskolin E (38)
H	OH	OAc	OH	Forskolin F(1-deoxyforskolin; coleonol D) (39)
OH	OAc	OAc	H	Forskolin G (40)
OAc	OAc	H	H	Forskolin H (41)
OAc	OAc	OH	OH	Forskolin I (42)
OH	OAc	OAc	OH	Forskolin J (6-O-acetylforskolin) (43)
OAc	OAc	OAc	H	1,6-Diacetoxy-9-deoxyforskolin (forskolin K) (44)
H	OH	H	H	6 $\beta$ -Hydroxy-8,13-epoxy-labd-14-en-11-one (forskolin L) (45)
H	OH	H	OH	Coleosol (46)
OAc	OH	H	OH	1-Acetoxycoleosol (47)
H	H	H	OH	Colcol (48)
H	H	H	H	11-Oxomanoyl oxide (49)
H	OH	$\alpha$ -OAc	H	Coleonol E (50)
H	OAc	$\alpha$ -OH	OH	Coleonol F (51)
OH	OH	$\alpha$ -OAc	H	Deoxycoleonol (52)

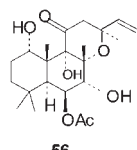
Fig. 2 8,13-Epoxy-labd-14-en-11-one diterpenoids.



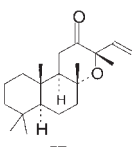
(53) R<sup>1</sup> = OH, R<sup>2</sup> = OAc 3-Hydroxyforskolin  
 (54) R<sup>1</sup> = OAc, R<sup>2</sup> = OH 3-Hydroxyisoforskolin



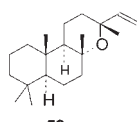
13-Epi-9-deoxycoleonol



Coleonol C

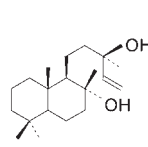


Coleonone

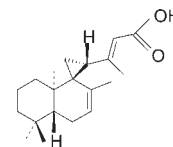


Manoyl oxide

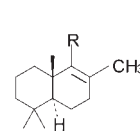
Fig. 3 8,13-Epoxy-labdane diterpenoids with some changes from the basic structure.



13-Epi-sclareol

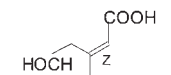


Forskoditerpene A

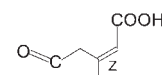


Compound

12-Hydroxy-8,13E-labdadien-15-oic acid (61)

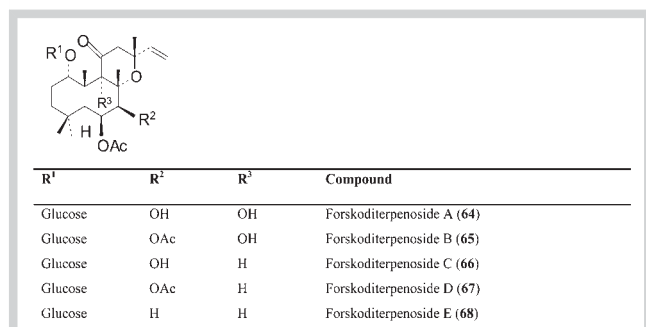


Coleolic acid (62)



Coleonic acid (63)

Fig. 4 Miscellaneous labdane diterpenoids.



**Fig. 5** 8,13-Epoxyabd-14-en-11-one diterpene glycosides.

nor 8,13-epoxy-labd-14-en-11-one diterpene glycosides such as forskoditerpenosides A (64), B (65), C (66), D (67), and E (68) were isolated from the whole plant of *P. barbatus* grown in China [61, 63] (Table 1, Fig. 5).

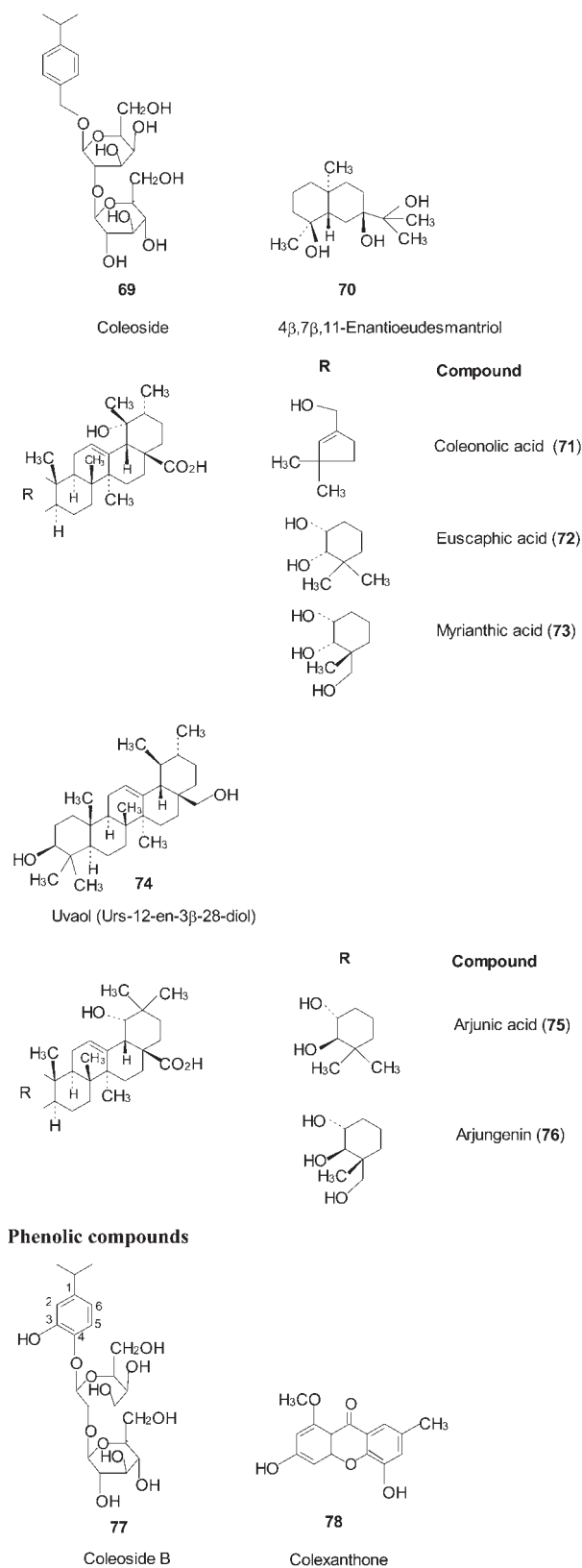
### Essential oils

The chemical composition of the essential oils of *P. barbatus* varied according to location and date of harvest, and contained mainly mono- and sesquiterpenes. The main constituents of the essential oil distilled from the leaves of *P. barbatus* grown in Brazil were  $\alpha$ -pinene, eremophyllene, myrcene, humulene,  $\beta$ -caryophyllene,  $\beta$ -o-cymene, limonene, nerolidol and farnesol [64, 65]. In addition, the diterpene manool (1.0%) was reported for the first time to be contained in the essential oil of the leaves [64]. In all, 91 components were detected in the essential oil obtained from the leaves of Rwandan *P. barbatus*. The main compounds were aromadendrene, borneol,  $\alpha$ -fenchyl acetate,  $\alpha$ -copaene,  $\gamma$ -2-cadinene, caryophyllene oxide, T-cadinol, calamene hydrate, and hydroxycalamene [66,67]. Steam distillation of the roots of *P. barbatus* grown in India and Brazil afforded an essential oil, the main constituents of which were found to be  $\beta$ -o-cymene, bornyl acetate, 3-decanone,  $\alpha$ -santalene,  $\alpha$ -pinene,  $\beta$ -pinene,  $\beta$ -caryophyllene, camphene, sabinene,  $\beta$ -ionone, (*E,E*)-farnesol,  $\alpha$ -cis-bergamotene and  $\gamma$ -curcumene [28,64]. Furthermore, the presence of the diterpene abietatriene (0.7%) (dehydroabietane) (19) (Fig. 1) was reported for the first time in the essential oil extracted from the roots of *P. barbatus* grown in Brazil [64]. Moreover, the essential oil of the stems of this plant afforded the major constituents,  $\beta$ -phellandrene,  $\alpha$ -pinene,  $\alpha$ -copaene, sabinene, caryophyllene oxide, limonene,  $\beta$ -caryophyllene, and  $\alpha$ -humulene [64].

### Miscellaneous constituents

The monoterpene glycoside coleoside (cuminylo- $\beta$ -D-glucopyranosyl-(1  $\rightarrow$  2)- $\beta$ -D-galactopyranoside) (69) [68], the sesquiterpenoids  $\alpha$ -cedrol [16,24] and 4 $\beta$ ,7 $\beta$ ,11-enantioeudesmantriol (70) [63], a number of pentacyclic triterpenoids of the ursane type such as  $\alpha$ -amyrin [24], coleonolic acid (2-hydroxymethyl-A-(1)-nor-urs-19 $\alpha$ -hydroxy-2(3),12(13)-dien-28-oic acid) (71) [69], euscaphic acid (2 $\alpha$ ,3 $\alpha$ 19 $\alpha$ -trihydroxyurs-12-en-28-oic acid) (72) [58], myrianthic acid (2 $\alpha$ ,3 $\alpha$ ,19 $\alpha$ ,23-tetrahydroxyurs-12-en-28-oic acid) (73) [58], and uvaol (urs-12-ene-3 $\beta$ -28-diol) (74) [30], of the lupane type such as betulinic acid [24], of the oleanane type such as arjunic acid (olean-12-en-28-oic acid,2 $\alpha$ ,3 $\beta$ ,19 $\alpha$ ) (75) [58] and arjungenin [2,3,19,23-tetrahydroxy-olean-12-en-28-oic acid (2 $\alpha$ ,3 $\beta$ ,4 $\alpha$ ,19 $\alpha$ )] (76) [58] (Fig. 6) as well as the tetrater-

### Other Terpenoids



**Fig. 6** Miscellaneous constituents.



**Table 2** Ethnobotanical uses of *Plectranthus barbatus*.

Digestive system	Respiratory system	Cardiovascular system
In India for abdominal colic [6]. For stomachache and as purgative in Kenya and for nausea in Southern Uganda [1, 74]. In Brazil, as a substitute for boldo ( <i>Peumus boldus</i> ) to treat gastric disturbances (e.g., gastritis and intestinal spasms) and hepatic disorders [1, 3, 29, 75]. Teeth and gum disorders [1].	Asthma, bronchitis, cold, cough and pneumonia [1, 4, 45, 66]. General respiratory ailments [1, 6, 74].	Angina, hemorrhage and hypertension [1, 6].
Nervous system	Pain, inflammation, musculoskeletal	Sensory
In Asia, for insomnia, convulsion [1, 6] and against dizziness and fluster [45]. In Tanzania for psychiatric problems [1].	Inflammation, abdominal and spasmodic pain, and painful micturition [1, 6]. Muscular, generalized pain, stiff neck, backache, bone dislocation, and rheumatism [1].	For conjunctivitis in Congo and earache in Kenya [1].
Skin	Metabolic & endocrine system	Infection
In East Africa (Kenya, Congo), for wounds and ringworms, to reduce swelling on bruises and as a bath for babies with measles [1, 74].	In Ayurvedic medicine for hypothyroidism [76]. As an emmenagogue, oral abortifacient [1, 77]. In Somalia as an aphrodisiac [1].	Throat and mouth infections, tonsillitis, gastrointestinal infections, genitourinary infections (e.g., syphilis in Central Africa) and eye and ear infections [1]. In Rwanda, Kenya, French Guiana and Brazil to treat malaria [1, 66, 78]. In Kenya for measles [74].

penoid crocetin dialdehyde [70] and the sterols {ergosterol endoperoxide (5 $\alpha$ ,8 $\alpha$ -epidioxy-ergosta-6,22-dien-3 $\beta$ -ol) [30], 5 $\alpha$ ,8 $\alpha$ -epidioxy-ergosta-6,9(11),22-trien-3 $\beta$ -ol [30], stigmasterol [16, 71], and  $\beta$ -sitosterol [16, 24, 30]} were isolated from different tissues of *P. barbatus* distributed in India and China.

Only one flavonoid and one phenylpropanoid, namely genkwainin (7-*O*-methylapigenin) and guaiacol glycerin ether, respectively, [16] as well as the phenolic compounds caffeic acid [68], coleside B (*p*-isopropylcatechol-4-*O*- $\beta$ -D-glucopyranosyl(1 $\rightarrow$ 2)- $\beta$ -D-galactopyranoside) (77) [72] and colexanthone (1-oxy-methyl-3,5-dihydroxy-7-methyl-xanthone) (78) [62] (● Fig. 6) were isolated from different parts of the Chinese and Indian *P. barbatus*. In addition three tetramethyl-substituted higher alkanes namely 2,6,10,14-tetramethylpentadecane, 2,6,10,14-tetramethylhexadecane, and 2,6,10,14-tetramethylheptadecane were isolated from the roots of the Indian *P. barbatus* [28]. Moreover, five glycolipids, such as monogalactosyl diacylglycerol, digalactosyl diacylglycerol, trigalactosyl diacylglycerol, tetragalactosyl diacylglycerol, and sulfoquinovosyl diacylglycerol were detected in the leaves of *P. barbatus* grown in Brazil [73].

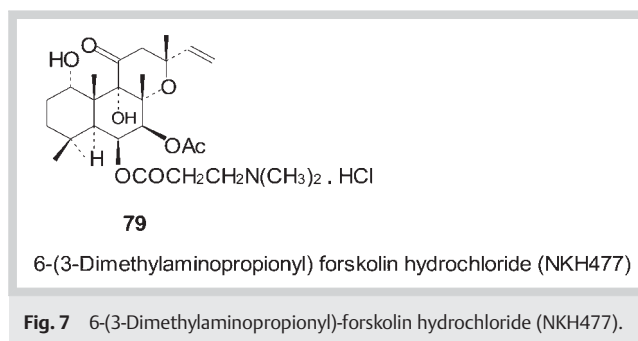
## Uses

### Ethnobotanical uses

*P. barbatus* has been used for centuries in Hindu and Ayurvedic traditional medicine as well as in the folk medicine of Brazil, tropical Africa and China for the treatment of various diseases [1, 3, 4, 6, 29, 45, 66, 74–78] (● Table 2). In addition, *P. barbatus* is used to alleviate fever in East Africa and India, as a children's tonic and also as an emetic utilized by the Samburu of Kenya for strength [1]. In Uganda the plant is used to treat spiritual ailments [79]. In Africa, the plant is applied in ethnoveterinary medicine, for instance in Kenya, it is used to treat Coast Fever in cattle [1]. *P. barbatus* is used against snakebites in India, Gabon and Kenya, and as insecticide to protect grain stores [1, 66].

### Non-medicinal uses

As reported by Lukhoba et al. [1], *P. barbatus* is planted as an ornamental and as a hedge, fence or boundary marker as well as soil improver for growing grains such as cowpeas, green grams and maize; it is also planted on the hillsides to prevent soil ero-

**Fig. 7** 6-(3-Dimethylaminopropionyl)-forskolin hydrochloride (NKH477).

sion and is used for making manure. The leaves of *P. barbatus* are cooked as a vegetable in Kenya and Yemen; it is fed to sheep, goats and cattle. In Kenya, the soft velvety leaves are used as sanitary tissue to clean milk guards and both the leaves and stems are used to hasten the ripening of bananas.

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