

A Detailed Review on Morphotaxonomy and Chemoprofiling of *Skimmia anquetilia*

N.P. Taylor and Airy Shaw

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In recent times, medicinal plants have attracted huge attention due to their diverse range of biological and therapeutic properties. Evidences have been accumulated since ages to demonstrate promising potential of medicinal plants used in various traditional, complementary, and alternative systems with the ever-increasing interest of today's population towards natural products, *Skimmia anquetilia* N.P. Taylor and Airy Shaw emerged out to be one of the most eye-catching plant bearing multiple medicinal properties. It is a perennial aromatic evergreen shrub belonging to family *Rutaceae*. Pharmacological studies have demonstrated significant action of different extracts as antimicrobial, anti-inflammatory agents, among others, supporting some of its popular uses. An attempt has been made in this review article to provide an up-to-date overview of the morphological parameters, taxonomic features, distribution pattern, traditional uses, as well as the phytochemistry and biological activities of *S. anquetilia*. The present review provides insights for future research aiming for both ethnopharmacological validation of its popular use and its exploration as a new source of herbal drugs and/or bioactive natural products.

Keywords: *Skimmia anquetilia*; *Rutaceae*; Phytochemistry; Taxonomy; Pharmacological Activity**Introduction**

Plant kingdom is a potential source of pharmaceutically active substances. In recent times the interest in plants rich in bioactive components has tremendously intensified due to their beneficial effects on human health. In last five decades, plants have been extensively studied by advanced scientific techniques and reported for various medicinal properties viz, anticancer activity, antibacterial activity, antifungal activity, antidiabetic activity, antioxidant activity, hepatoprotective activity, haemolytic activity, larvicidal activity and anti-inflammatory activity [1,2].

Skimmia anquetilia N. P. Taylor and Airy Shaw commonly known as Himalayan *Skimmia*, a member of the family *Rutaceae*, endemic to Western Himalaya is distributed in the mountain ranges of Kashmir Himalaya confined to shady regions under forests in association with conifers, grassy and rocky slopes ranging in altitude from 1800 - 2715m. Locally, it is known as "Naer". It has a tremendous medicinal importance and as such adds beauty to the crown of Himalaya.

The present review aims to document the distribution, morphology, taxonomy, traditional uses, phytochemistry and biological activities of *S. anquetilia* and its future prospects for the further scientific investigation for the development of effective therapeutic compounds.

Distribution

The family *Rutaceae* predominantly consisting of trees and shrubs, is prevalent in tropical and temperate regions of the world.

It is distributed in South East Asia, Mediterranean countries, North America, Australia and South Africa [3]. The family consists of @150 - 162 genera with @1500 - 2096 species having three major centers of diversity: Tropical America, Southern Africa, and Australia [4,5]. In Kashmir Himalaya, the family is represented by 4 genera and 6 species, (wild and cultivated) [6] (Table 1).

Family	Genera	Species
<i>Rutaceae</i>	<i>Citrus</i>	* <i>Citrus reticulata</i>
		* <i>Citrus sinensis</i>
	<i>Dictamnus</i>	<i>Dictamnus alba</i>
	<i>Skimmia</i>	<i>Skimmia anquetilia</i>
<i>Zanthoxylum</i>	<i>Zanthoxylum armatum</i>	

Table 1: Status of family *Rutaceae* in Kashmir Himalaya [6]

*Cultivated

Genus *Skimmia* Thunb., one of the genera of family *Rutaceae*, is distributed in the Himalayas, E. Asia, Japan and Phillipine Islands [7]. Hooker [8], reported four species of *Skimmia* from Himalaya and Japan. As per Taylor [9] the genus *Skimmia* includes four well defined species, three of which are divided into two sub-species (Table 2). Dianxiang and Hartley [10] reported five species of genus *Skimmia* from China with one of the species endemic to the region table 3. In Kashmir Himalaya, the genus *Skimmia* is represented by a single species i.e. *Skimmia anquetilia* [6].

Genus	Species	Sub-species
<i>Skimmia</i>	<i>S. japonica</i>	<i>S. japonica</i> subsp. <i>japonica</i>
		<i>S. japonica</i> subsp. <i>reevesiana</i>
	<i>S. laureola</i>	<i>S. laureola</i> subsp. <i>laureola</i>
		<i>S. laureola</i> subsp. <i>multinervia</i>
	<i>S. arborescens</i>	<i>S. arborescens</i> subsp. <i>arborescens</i>
		<i>S. arborescens</i> subsp. <i>nitida</i>
<i>S. anquetilia</i>	—	

Table 2: Status of genus *Skimmia* in world [9].

S. No.	Name of the species	Habitat	Altitude(m) asl
1.	<i>Skimmia reevesiana</i>	Montane moss forests	1200 - 2600
2.	<i>Skimmia melanocarpa</i>	Dense or open forests	2000 - 3000
3.	<i>Skimmia laureola</i>	Evergreen forests	Below 2800
4.	<i>Skimmia arborescens</i>	Shady moist montane forests	1000 - 2800
5.	<i>Skimmia multinervia</i>	Montane forests	2800 or above

Table 3: Status of genus *Skimmia* in China [10].

Skimmia anquetilia is distributed in West Asia: Afghanistan and Indian sub-continent: India, Pakistan and Nepal. In India, it grows in Uttar Pradesh, Jammu and Kashmir and Himachal Pradesh [11,12]. As per KASH (Kashmir University Herbarium), it is distributed in Sonmarg, Yusmarg, Gulmarg, Tangmarg, Aharbal, Duksum, Hillar nar.

Morphological and Taxonomic Description

Genus *Skimmia*, one of the genera of family *Rutaceae*, distributed in the Himalayas, E. Asia, Japan and Phillipine Islands, is characterized by a strong musky smell [13]. The botanical description of the genus *Skimmia* is given in table 4.

<i>Skimmia</i>	Habit	Evergreen, shrubs or trees
	Leaves	Simple; petiolate; alternate; glandular-punctate
	Inflorescence	Terminal, thyriform.
	Flower	Polygamous. Sepals 3 - 4 or 5 - 7, distinct or basally connate; petals 3 - 4 or 5 - 7, imbricate in bud; stamens 3 - 4 or 5 - 7, distinct, rudimentary in female flower; disk annular or pulvinate.; ovary 2 - 5 -loculed, syncarpous, rudimentary in male flowers, style stout or absent.
	Fruit	Fleshy drupaceous berry (1 - 5) 1-seeded leathery pyrenes
	Seed	Ovoid to ellipsoid; seed coat membranous; endosperm copious; embryo straight; cotyledons oblong to suborbicular, flattened; hypocotyl superior

Table 4: Botanical features of Genus *Skimmia* [13].

At generic level, *Skimmia* has a taxonomic confusion. As per Taylor [9] genus *Skimmia* consists of only four well-defined naturally-occurring species, three of which have two sub-species (Table 5) but Dianxiang and Hartley [10] reported 5 species based on the following taxonomic key:

Classification by Taylor (1987)	Classification by Dianxiang and Hartley (2008)
<i>Skimmia japonica</i> subsp. <i>japonica</i>	-
<i>S. japonica</i> subsp. <i>reevesiana</i>	<i>S. reevesiana</i>
<i>S. laureola</i> subsp. <i>laureola</i>	<i>S. melanocarpa</i>
<i>S. laureola</i> subsp. <i>multinervia</i>	<i>S. multinervia</i>
<i>S. arborescens</i> subsp. <i>arborescens</i>	<i>S. arborescens</i>
<i>S. arborescens</i> subsp. <i>nitida</i>	-
<i>S. anquetilia</i>	-
-	<i>S. laureola</i>

Table 5: Comparative classification given by Taylor [9] and Dianxiang and Hartley [10].

- 1a. Leaf blade mid-vein puberulent.
- 2a. Fruit red1. *S. reevesiana*
- 2b. Fruit bluish black2. *S. melanocarpa*
- 1b. Leaf blade midvein glabrous.
- 3a. Leaf blade secondary veins 12 - 20 on each side of midvein; rudimentary gynoecium in male flowers entire or nearly so; petals reflexed5. *S. multinervia*
- 3b. Leaf blade secondary veins fewer than 10 on each side of midvein; rudimentary gynoecium in male flowers 3- or 4 - lobed; petals erect to spreading.
- 4a. Shrubs to 2m tall; fruit red 3. *S. laureola*
- 4b. Trees to 12m tall; fruit bluish black4. *S. arborescens*

International Plant Names Index (2014) listed 31 *Skimmia* species in the World (excluding hybrids and intraspecific entities) [14] (Table 6).

S. No.	<i>Skimmia</i> species
1.	<i>Skimmia anquetilia</i> N. P. Taylor and Airy Shaw
2.	<i>Skimmia arborescens</i> T. Anderson ex Gamble
3.	<i>Skimmia arisanensis</i> Hayata
4.	<i>Skimmia distincte-venulosa</i> Hayata
5.	<i>Skimmia euphlebica</i> Merr.
6.	<i>Skimmia foremanii</i> H. Knight
7.	<i>Skimmia formosana</i> C.E.Chang
8.	<i>Skimmia fragrantissima</i> Hort. ex T.Moore
9.	<i>Skimmia fortunei</i> Mast.
10.	<i>Skimmia fragrans</i> Carrière
11.	<i>Skimmia hainanensis</i> C.C.Huang
12.	<i>Skimmia intermedia</i> Carrière
13.	<i>Skimmia japonica</i> Thunb.
14.	<i>Skimmia kamengensis</i> Goel and Mehrotra,
15.	<i>Skimmia kwangsiensis</i> C.C.Huang
16.	<i>Skimmia laureola</i> (DC.) Decne.
17.	<i>Skimmia lutchuensis</i> Nakai

18.	<i>Skimmia melanocarpa</i> Rehder and E.H.Wilson
19.	<i>Skimmia multinerva</i> C.C.Huang
20.	<i>Skimmia oblata</i> T.Moore
21.	<i>Skimmia orthoclada</i> Hayata
22.	<i>Skimmia ovata</i> Hort.exLavallée
23.	<i>Skimmia philippinensis</i> Masam
24.	<i>Skimmia reevesiana</i> R.Fortune
25.	<i>Skimmia repens</i> Nakai
26.	<i>Skimmia rogersii</i> Hort.
27.	<i>Skimmia rubella</i> Carrière
28.	<i>Skimmia rugosa</i> Makino
29.	<i>Skimmiaveitchii</i> Carrière, and
30.	<i>Skimmia wallichii</i> Hook f. and Thomson ex Gamble
31.	<i>Skimmia arunachalensis</i> Goel and Mehrotra

Table 6: List of *Skimmia* species in the World as per International Plant Index (2014) [14].

As per Ling [15] the genus *Orixa* is closer to the genus *Skimmia* and both genera together form a well-supported clade with the genus *Dictamnus* [16] and further this close relation to *Dictamnus* was confirmed and the genus *Skimmia* placed in subfamily *Rutoideae* while it was formerly placed in *Toddalioidea* [17].

Skimmia anquetilia is an aromatic erect or creeping shrub. The plant is about 1.5m long and densely branched. *S. anquetilia* bears fruits in terminal fascicles during July-November. The fruits are pedicellate, ovoid bright red, 7 - 15 mm long with 1 - 2 stones (endocarps), each bearing one seed. Seeds are albuminous, testa membranous, cotyledons rounded to oblong; yellowish [18].

The investigation on *S. anquetilia* revealed extensive variability in morphological parameters both within and across the individuals of different populations. The plants growing at low altitudes are comparatively much more diverse and vigorous. Also, the partitioning of resources is not even among different parts of the plant, wherein much resources are allocated towards the root followed by shoot, leaves and least amount towards the inflorescence [19]. The morphological parameters of *S. anquetilia* are summarized in table 7.

Traditional Uses

Skimmia anquetilia is a medicinal plant widely used in traditional system of medicine. In Indigenous system of medicine, the roots of this plant are used as an antidote to snake bite and scorpion bite while the dried leaves are used as an insecticide, pesticide and in the treatment of cold, fever and headache [20]. The leaves of *S. anquetilia* along with curcuma are mixed to prepare a paste, which is considered to be effective against rheumatic pains and swellings and its powdered bark is used for the healing of burns and wounds [21,22]. A high caloric Indian traditional alcoholic beverage is prepared with leaves of *S. anquetilia* [23]. The fresh leaves are used in the treatment of smallpox [18].

Phytochemistry

Genus *Skimmia* is a rich source of secondary metabolites which includes alkaloids, coumarins, limonoids, cholestane derivatives, triterpenes, flavonoids and unusual fatty acid derivatives [14]. *Skimmia* is used in traditional system of medicine against fever, inflammation and rheumatism [14]. Various species of genus *Skimmia* are associated with activities like antibacterial, antifungal and antifeedant [24,25].

Sharma, *et al.* [26,27] extracted six coumarins using ethanolic extract of leaves of *S. anquetilia* which include (7,8-dihydroxy-6-[3'- β -D-glucopyranosyloxy-2'-hydroxy-3'-methylbutyl] coumaringlucosid; 6-(2,3 dihydroxy-3-methylbutyl)-7-methoxycoumarin; skimmine; osthol; esculetin and scopoletin.

The essential oils obtained by hydro-distillation from its seeds and fruits of *S. anquetilia* and analysed by GC-MS contained up to 70 compounds and revealed the dominance of fatty acids and esters of fatty acids. However, α -cadinol, α -terpineol, selinene, neoisolongifolene, linalool, cis-Z- α -bisabolene oxide, aromadendrene, and (-)-selinene were the main points of differences between the two essential oils [18]. On the other hand, Gondwal, *et al.* [28,29] using the same methodology as above indicated, but analyzing the essential oils of flowers and leaves of *S. anquetilia*, showed the presence of β -phellandrene (1.8% in leaves and 18.4% in flowers), geijerene (2.0%, 15.0%), germacrene B (11.6%, 2.0%), linalyl acetate (7.3%, 11.2%), linalool (9.5%, 9.4%), α -terpineol (5.6%, 4.4%), and pregeijerene (0.2%, 5.6%) as the most abundant mono- and sesquiterpenes.

The leaves of *S. anquetilia* are aromatic and known to contain linalool, geraniol, pinene, scopoletin, skimmianine, umbelliferone [30].

Pharmacological Activity

Antioxidant

Gondwal, *et al.* [28] assessed the antioxidant activities of water extracts and essential oils isolated from leaves and flowers of *S. anquetilia* using different methods to compare effects on redox potential, chelating properties on Fe^{2+} and 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging ability. The essential oil and water extract from flowers displayed the maximum chelating activity. The maximum reducing power was exhibited by flower essential oil and leaf extract. The highest DPPH radical scavenging potential was observed in leaf essential oil and leaf extract.

Prakash, *et al.* [18] using the same assays to evaluate water extracts from seeds and fruit pulp of *S. anquetilia* found that both the extracts showed moderate antioxidant power, with fruit pulp being more effective in all activities than seeds. The ability of fruit pulp to scavenge DPPH radicals was similar to that of flower and leaf extracts [28,29].

John, *et al.* [31] evaluated the antioxidant potential of various organic-methanol, n-hexane, dichloromethane, ethyl acetate, butanol and aqueous fractions from leaves of *S. anquetilia* using eight different methods- 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) radical cation scavenging activity, the ferric reducing antioxidant power (FRAP), 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, total phenolic contents (TPC), total flavonoid contents (TFC), total antioxidant activity by phosphomolybdenum method, superoxide anion radical scavenging activity and metal chelating activity. They opined that the ethyl acetate fraction showed the highest total phenolic content, 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) radical cation scavenging activity, the ferric reducing antioxidant power (FRAP), and the DPPH radical scavenging activity. Dichloromethane fraction showed the highest antioxidant activity. The highest superoxide anion radical scavenging activity was displayed by the aqueous fraction. Crude methanolic extract exhibited highest total flavonoid contents as well as highest.

Anti-inflammatory

Kumar, *et al.* [32] evaluate the effects of different leaf extracts of *S. anquetilia* on human red blood cell membrane stabilization and on carrageenan-induced paw edema in rats and used diclofenac (10 mg/kg) as a positive control compound. Percentages of protection provided by samples in the *in vitro* membrane-stabilizing test increased in the following order: petroleum ether (PE), aqueous (AE), chloroform (CE), ethyl acetate (EE), and methanol (ME) extracts. In an *in vivo* model, the percentage of inhibition of inflammation of CE, EE, and ME showed the same order of increase. In both cases, methanol extract (400 mg/kg) was found to be the most potent ($p < 0.01$) with significant anti-inflammatory activity, slightly lower than that of diclofenac (inhibitions of 68.4% vs. 74.2% and 67.5% vs. 71.6%, respectively).

Antibacterial

Sharma, *et al.* [26,27] revealed that methanolic extract of *S. anquetilia* and 7,8-dihydroxy-6-[3'- β -D-glucopyranosyloxy-2'-hydroxy-3'-methylbutyl]-coumarin isolated from *S. anquetilia* are active at high concentrations of 200 μ g/disc against three Gram-negative plant pathogens viz., *Agrobacterium tumefaciens*, *Pseudomonas syringae* and *Pactobacterium carotovorum*, while skimming was found effective only against *A. tumefaciens*.

Antifeedant

Negi, *et al.* [33] showed that *S. anquetilia* possess potent anti-feedant properties as its extract has been proven effective against forest pests (Lepidoptera).

Gondwal, *et al.* [29] concluded that the essential oils of flowers and leaves of *Skimmia anquetilia* suppressed egg laying capability of *Caryedon serratus*. This suppression increases with the increase in concentration of oil but no effect on further development of eggs to adults was observed.

Conclusion

It is quite evident from this review that *S. anquetilia* contains a number of bioactive compounds, which are the key factors in the medicinal value of this plant. Numerous studies have been conducted on different parts of this plant, but till today, the plant has not been developed or commercialized as suitable drugs by pharmaceutical industries. This review has presented a comprehensive view about the morphology and phytochemistry of *S. anquetilia*. However, the research is very limited in some areas and further study on phytochemicals and their mode of actions revealing pharmacological effects are required to fully understand in concern with the traditional uses. In addition, the pharmacological experiments performed in the plant must be extended to the next level of clinical trial to generate novel drugs. This might prove helpful to use its immense therapeutic efficacy as a potent phytomedicine. Therefore, a systemic research and development work should be undertaken for the development of products for their better economic and therapeutic utilization.

Conflict of Interest Statement

We declare that we have no conflict of interest.

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