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Review

A review of phytochemistry, bioactivities and ethno medicinal uses of *Rhazya stricta* Decsne (Apocynaceae)

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***Rhazya stricta* Decne is an important medicinal plant belonging to family Apocynaceae. Its chemical constituents, biological and pharmacological activities, and ethno medicinal uses have been reviewed in the present study. The reported phytochemical studies conducted on various parts of *R. stricta* plant revealed presence of over 100 alkaloids and few non-alkaloidal compounds. Most of the activities of the plant reside in its alkaloidal fractions. The compounds have been reported to exhibit ambulatory, antifungal, antimicrobial, antioxidant, endogenous monoamine oxidase (MAO) A and B inhibitory and herbicidal activities. They also showed effects on arachidonic acid (AA) metabolism, blood pressure, central nervous system (CNS), immunity, smooth muscles and glucose homeostasis. Different parts of the plant have been reported to be used in traditional medicine against various ailments such as diabetes, foot burning, skin diseases, stomach pain etc. But more work needs to be done regarding its medicinal importance (recording and exploring recipes) for the benefit of improving human health. As the plant of *R. stricta* has immense potential as an anti-microbial due to its richness of phytochemicals it possesses, therefore, such studies are recommended in various parts of the countries of Arabian Peninsula and the Indian subcontinent where it grows**.

Key words: Photochemistry, bioactivities*, Rhazya stricta,* apocynaceae.

INTRODUCTION: *RHAZYA STRICTA* DECAISNE

The genus Rhazya (family Apocynaceae) comprises two species, namely *Rhazya stricta* Decaisne and *Rhazya orientalis* (Ali et al., 2000a). *Rhazya spp* were called after the name of a Muslim scientist Abu Bakr Mohammed bin Zakariya Ar-Razi (925), known in Europe mostly under the Latinized name of Rhazes (Batanouny et al., 1999).

Description

R. stricta is a small glabrous, erect under shrub or shrub about 90 cm high (Jafri, 1966), with a smooth central stem and dense semi-erect branches (Western, 1989); leaves alternate, 6 to 10 × 1 to 2 cm, elliptic–lanceolate, thick or leathery, sessile, turning yellow with age; flowers white in short branched cymes; fruit pale yellow follicles; seeds shortly winged (Jafri, 1966).

Vernacular names

It is known as 'Rangobul' in Urdu, 'Vergalum', Ganderi in Pushto (Ali et al., 2000b) and harmal in Arabic, however, one should distinguish between the harmal for *Peganum harmala* and the harmal for *R. stricta* in Arabic countries (Batanouny et al., 1999).

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Distribution

R. stricta is an important medicinal species used in indigenous medicinal herbal drugs to cure various ailments in Pakistan, India and Afghanistan, Saudi Arabia, Qatar, United Arab Emirates (UAE), Iran and Iraq (Gilani et al., 2007).

Several phytochemical studies conducted on various parts of *R. stricta* plant have revealed presence of over 100 alkaloids (Ahmad et al.,1983; Ali et al., 2000a; Atta-ur-Rahman and Khanum,1985; Atta-ur-Rahman and Zaman,1986; Atta-ur-Rahman et al., 1986; Atta-ur-rahman et al., 1996; Banerji et al., 1970; Bashir et al., 1994; Fatima et al,1980; Habib-ur-Rehman,1987;Habib-ur-Rehman and Atta-ur-ahman,1996; Mariee et al.,1988; Mukhopadhayay et al.,1981; Mukhopadhayay et al., 1983; Qureshi,1991; Saeed et al., 1993). In addition to alkaloids, isolation of some non-alkaloidal compounds has also been reported from *R. stricta* plant (Zaman, 1990; Sultana and Khalid, 2010). (Figure 1)

The plant is used in UAE, mostly in the form of decoctions, for a variety of unrelated illnesses that include diabetes mellitus, fever, sore throat, inflammatory conditions and helminthiasis (Al Gonemi, 1992). In the rural areas of Saudi Arabia, the leaves of *R. stricta* are used in folk medicine as a reputed bitter tonic and a curative for syphilis (Ali et al., 2000b), chronic rheumatism, and similar types of pains (Al-Yahya et al., 1990), powder of dried fresh leaves is taken with water for pimples and acne problem of face. Fresh leaves are kept in shoes and put under feet for foot burning. Branches are used as toothbrush for teeth ache (Sultana et al., 2006). The paste of soaked seeds with butter used for achenes and the removal of the heat effects (Qureshi et al., 2007).

A good amount of work regarding pharmacological, phytochemical, toxicological and to some extent biological activities of *R. stricta* has been reported (Atta-ur-Rahman and Fatima, 1982; Atta-ur-Rahman et al., 1989; Chatterjee et al., 1974; Ali et al., 2000a). (Table 3) But more work needs to be done regarding its medicinal importance, taxonomic and ecological aspects. As the plant of *R. stricta* has immense potential as an anti-microbial due to the rich source of phytochemicals it possesses, therefore, such studies on biological activities particularly anti microbial are recommended in various parts of the countries of Arabian Peninsula and the Indian subcontinent where it grows.

Phytochemistry

There is a plethora of studies on the phytochemical constituents of the leaves, fruits, legumes and roots of *R. stricta*. Over 100 alkaloids a few flavonoids have been isolated and their structure elucidated, mainly from the leaves but also from other parts of *R. stricta* found in India, Pakistan, Saudi Arabia and the United Arab Emirates (Ali et al., 2000a). Chemical constituents of *R. stricta* with their formulae, molecular weight obtained from some selected studies have been summarized in the Table 1 for convenience.

Medicinal uses

R. stricta is an important medicinal plant used in indigenous medicinal herbal drugs to cure various ailments in various countries. It is used in fever, general debility and as curative for chronic rheumatism and tumor. *R. stricta* is used traditionally in Asia for the treatment of different types of diseases such as skin diseases, stomach diseases and antihypertensive. The leaves, flowers and fruit are also used in joint infections and for cancer (Khan and Khan, 2007). Table 2 summarizes the data obtained from some selected studies.

Biological and pharmacological activities

Ambulatory activity

The effect of acute and chronic treatment of rats with a lyophilized extract of the leaves of *R. stricta* on total and ambulatory activity was studied. Given acutely at single oral doses of 1, 2, 4, and 8 g/kg_body weight, the extract produced dose-dependent decreases in total activity and ambulatory activity. Diazepam (20 mg/kg p.o.) produced a decrease in rat activity comparable to that produced by a dose of 1 g/kg of the extract. When given daily at an oral dose of 2 g/kg for 21 consecutive days, the extract produced, on the last day of treatment, significant decrease in activity amounting to about 30% of control activity levels (Ali et al., 1999).

Antibacterial and antifungal activities

The crude ethanolic extract of *R. stricta* fruit has led to the determination of good results of antibacterial, lipoxygenase and acetylcholinesterase activities (Sultana and Khalid, 2010).The chloroform and methanol extracts of the roots of *R. stricta*, showed antimicrobial and antifungal activities against *Staphylococcus aurous*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Aspergillus terreus*, *Aspergillus flavus* and *Candida albicans*. Tetrahydrosecamine, isolated from the plant showed broad spectrum antimicrobial activity (active against all except *E. coli*; MIC values 0.1 to 5.0 mg/ml). Similarly, another active component, Strictanol, was also found to be most active against *E. coli* and *P. aeruginosa* (MIC 0.5 mg/ml for both organisms) (Bashir et al., 1994).

Figure 1. Rhazya stricta: A. Shoot of the plant, B. Flowers, C. Fruit (follicles) and D. Seeds Source:http://www.google.com.pk/search?hl=en&cp=5&gs_id=i&xhr=t&q=rhazya+stricta&biw=1024&bih=600&gs_sm=&gs_upl=&wrapid=tljp1314514464812 08&um=1&ie=UTF-8&tbm=isch&source=og&sa=N&tab=wi

In vitro antifungal study was performed by subjecting different microorganisms to various fractions of *R. stricta* in different solvents. Five fractions were used in the studies named pet ether, carbon tetra chloride, chloroform, ethyl acetate and methanol. Among these, methanol and chloroform fractions showed significant antifungal activities. Petroleum ether and carbon tetrachloride fractions showed low activities against the said organisms, while ethyl acetate fraction no activity at all (Khan and Khan, 2007).

Antioxidant action

R. stricta has been shown to have an antioxidant action in rats (Ali, 2002). The methanolic extract of *R. stricta* leaves exhibited the highest total phenolic content and an antioxidant potential which was comparable with previously exploited potent antioxidants (Iqbal et al., 2006). The crude ethanolic extract of *R. stricta* fruit has also shown good results of lipoxygenase and acetylcholinesterase activities (Sultana and Khalid, 2010).

Antineoplastic activity

Tetrahydrosecamine and 16-epi-Z-isositsirikine, isolated from this plant, also displayed antineoplastic activity in KB test system *in vitro* and P-388 test system *in vivo* (Zaman, 1990).

Cytotoxic activity

Cytotoxicity of active components of this plant has been evaluated against the cell cultures of Eagle's KB of the human carcinoma of the nasopharynx and lymphocyte carcinoma of the mouse P-388. Vallesiachotamine has shown moderate *in vivo* cytotoxic activity (Zaman, 1990).

Effect on central nervous system

The effects of orally administered aqueous lyophilized extract of the leaves of *R. stricta* (2, 4 and 8 g/kg) on aspects of nervous system function were investigated in mice. The extract exhibited significant dose-dependent

Table 1. Chemical composition of *Rhazya stricta* Decne. reported from literatures.

Compound	MF	MW	Part	Reference
Alkaloids				
Akuammidine,	$C_{21}H_{24}N_2O_3$	352	Lf	Bashir et al. (1994); Fatima (1980); Zaman (1990)
Alkaloid R_1	$C_{21}H_{24}N_2O_3$	352	Lf	Qureshi (1991); Zaman (1990)
Alkaloid R_2	$C_{21}H_{22}N_2O_3$	350	Lf	Habib -UR -Rehman (1987); Qureshi (1991)
Alkaloid R_3	$C_{21}H_{22}N_2O_3$	350	Lf	Habib -UR -Rehman (1987); Qureshi (1991)
Antirhine	$C_{19}H_{24}N_2O$	296	Lf	Habib-UR- Rehman (1987); Qureshi (1991); Banerji et al. (1970); Zaman (1990)
3-epi- Antirhine	$C_{19}H_{24}N_2O$	296	Lf	Habib- UR- Rehman (1987)
Aspidospermiose	$C_{24}H_{32}N_2O_5$	428	Lf	Habib-ur-Rehman and Atta-ur-Rahman (1996)
Aspidosespermidine	$C_{19}H_{26}N_2$	282	Lf	Habib- UR- Rehman (1987); Fatima (1980)
Bhimberine-N-oxide	$C_{21}H_{26}N_2O_4$	370		Qureshi (1991)
Bhimberine	$C_{21}H_{26}N_2O_3$	354		Qureshi (1991)
Bis-strictidine	$C_{38}H_{48}N_4$	556	Lf	Habib-UR- Rehman (1987); Qureshi (1991)
Condylocarpine	$C_{20}H_{22}N_2O_2$	322	Fr	Qureshi (1991)
16S, 16'-Decarboxytetra-hydrosecamine	$C_{40}H_{54}N_4O_2$	622	--	Qureshi (1991)
Decarbomethoxy-15,20,16,17-tetrahydrosecodine		284	--	Qureshi (1991)
1,2-Dehydroaspidosperm-idine (eburenine)	$C_{19}H_{24}N_2$	280	Lf	Fatima (1980); Habib-ur- Rehman (1987); Qureshi (1991)
1,2-Dehydroaspidosperm-inine-N-oxide	$C_{19}H_{24}N_2O$	296	Lf, Rt	Habib- UR- Rehman (1987) Atta-ur-Rahman and Zaman (1984,1986)
3, 14-Dehydrorhazigine	$C_{40}H_{48}N_4O_2$	616	Lf	Habib-UR- Rehman (1987); Qureshi (1991)
Didemethoxycarbonyl-1-Carboxymethoxy-b-carboline	$C_{13}H_{10}N_2O_3$	226	Lf	Habib-ur-Rehman and Atta-ur-Rahman (1996)
Dihydrocorynantheol	$C_{19}H_{26}N_2O$	298	Lf	Habib -UR- Rehman (1987); Qureshi (1991)
Dihydroebumamenine	$C_{19}H_{24}N_2$	280	--	Qureshi (1991)
Dihydropresecamine	$C_{42}H_{54}N_4O_4$	678	Lf	Habib- UR –Rehman (1987); Qureshi (1991)
Dihydrosecamine	$C_{42}H_{54}N_4O_4$	678	Lf	Habib -UR –Rehman (1987);Qureshi (1991); Fatima (1980)
Dihydrosecodine	$C_{21}H_{28}N_2O_2$	340	Lf	Habib -UR –Rehman (1987); Qureshi (1991); Fatima, (1980)
Eburnamenine	$C_{19}H_{22}N_2$	278	Lf	Habib-UR- Rehman (1987); Fatima (1980)
21S-Ebumamenine	$C_{19}H_{22}N_2$	278	--	Qureshi (1991)
Eburnamine(pleiocarpinidine)	$C_{19}H_{24}N_2O$	296	Lf	Habib- UR –Rehman (1987); Qureshi (1991); Fatima (1980)
Eburnamonine	$C_{19}H_{22}N_2O$	294	Lf	Habib- UR –Rehman (1987); Qureshi, 1991; Fatima, (1980)

Table 1. Contd.

16-Formylstrictamine	$C_{21}H_{22}N_2O_3$	350	Lf	Fatima,1980
Geissoschizine	$C_{21}H_{24}N_2O_3$	352	Lf	Habib- UR- Rehman (1987); Qureshi (1991); Banerji et al. (1970); Fatima (1980)
Harhingine	$C_{19}H_{20}N_2O$	292	Lf	Ali et al. (2000a)
15b-Hydroxyvincadifformine	$C_{21}H_{26}N_2O_3$	354	Lf	Ali et al. (2000a); Qureshi (1991)
16,hydroxyrhazisidine	$C_{40}H_{48}N_4O_3$	632	Lf	Habib- UR –Rehman (1987); Qureshi (1991)
Isorhazicine	$C_{21}H_{24}N_2O_4$	368	Lf	Habib- UR –Rehman (1987); Qureshi (1991); Ali et al. (2000a)
Isositsinkine	$C_{21}H_{26}N_2O_3$	354	--	Qureshi (1991)
16-*Epi*-Z-isositsirikine	$C_{21}H_{26}N_2O_3$	354	Lf	Mukhopadhayay et al.(1983); Habib- UR- Rehman (1987); Qureshi (1991)
Isovelasiachotamine	$C_{21}H_{22}N_2O_3$	350	Lf	Habib-UR- Rehman (1987); Qureshi (1991)
Leepacine	$C_{21}H_{22}N_2O_3$	350	--	Qureshi (1991)
Leuconolam	$C_{19}H_{22}N_2O_3$	326	Lf	Khanum (1986); Qureshi (1991)
2-Methoxy 1,2- dihydorhazimine	$C_{22}H_{26}N_2O_4$	382	Lf	Atta-ur-Rahman and Khanum (1985); Habib- ur- Rehman (1987)
17-Methoxy 1, 17-dihydorhazimine	$C_{22}H_{26}N_2O_4$	382	--	Qureshi (1991)
16R,21R-O-Methylebumamine	$C_{21}H_{25}N_2O$	310	--	Qureshi (1991)
N-Methyleuconulam	$C_{20}H_{24}N_2O_3$	340	--	Qureshi (1991)
Nor-C-luorocurarine	$C_{19}H_{20}N_2O$	292	--	Qureshi (1991)
Norfluorocurarine	$C_{19}H_{20}N_2O$	292	Lf	Fatima (1980); Habib-ur- Rehman (1987)
Nb-methyl strictamine			Lf	Atta- ur-Rahman et al. (1987b)
Quebrachamine	$C_{19}H_{26}N_2$	282	Lf	Habib- UR –Rehman (1987); Fatima (1980); Zaman (1990)
Polyneuridine	$C_{21}H_{24}N_2O_3$	352	Lf, Rt	Habib ur Rehman, 1987; Zaman,1990; Qureshi, 1991; Ali et al., 2000
Rhazicine	$C_{21}H_{24}N_2O_4$	368	Lf	Khanum, 1986; Habib UR Rehman, 1987; Qureshi,1991
Rhazidigenine-N-oxide	$C_{19}H_{26}N_2O_2$	314	Lf	Habib UR Rehman, 1987; Qureshi,1991
Rhazidine (Rhazidigenine)	$C_{19}H_{26}N_2O$	298	Lf,Rt	Habib- ur- Rehman (1987); Zaman (1990); Qureshi(1991); Fatima (1980)
Rhazigine	$C_{40}H_{50}N_4O_2$	618	Lf	Habib -UR –Rehman (1987); Qureshi (1991)
Rhazimal (16,Formylstrictamine)	$C_{21}H_{22}N_2O_3$	350	Lf	Habib -UR –Rehman (1987); Ahmad et al. (1983); Fatima (1980)
Rhazimanine	$C_{21}H_{26}N_2O_3$	354	Fr	Atta-ur-Rahman et al. (1986); Qureshi (1991)
Rhazimidine	$C_{21}H_{26}N_2O_3$	354	Lf	Habib -UR- Rehman (1987)
Rhazimine	$C_{21}H_{22}N_2O_3$	350	Lf	Habib- ur –Rehman (1987); Qureshi (1991); Saeed et al. (1993)
Rhaziminine			Lf	Bashir et al. (1994a)
Rhazimol	$C_{21}H_{24}N_2O_3$	352	Lf	Habib-UR- Rehman (1987); Qureshi (1991); Ahmad et al. (1983); Fatima (1980)
Rhazinol (a hydroxymethyl analogue of strictamine),			Lf	Ahmad et al. (1983); Fatima (1980)
Rhazinaline	$C_{21}H_{22}N_2O_3$	350	Lf	Habib -UR –Rehman (1987); Qureshi (1991); Fatima (1980)

Table 1. Contd.

Rhazind	$C_{19}H_{22}N_2O$	294	--	Qureshi (1991)
Rhazinilam	$C_{19}H_{22}N_2O$	294	Lf	Habib -UR –Rehman (1987); Qureshi (1991); Fatima (1980)
Rhazinine	$C_{19}H_{24}N_2O$	296	Lf	Zaman (1990)
Rhazisidine	$C_{40}H_{46}N_4O_2$	614	Lf	Habib -UR –Rehman (1987); Qureshi (1991)
Rhazizine	$C_{21}H_{24}N_2O_4$	368	--	Qureshi (1991)
Secamine	$C_{42}H_{52}N_4O_4$	676	Lf	Habib- UR -Rehman (1987); Qureshi (1991); Fatima (1980)
Presecamine	$C_{42}H_{52}N_4O_4$	676	Lf	Habib- UR –Rehman (1987); Qureshi (1991); Fatima (1980)
Sewarine	$C_{20}H_{22}N_2O_3$	338	Lf, Rt	Fatima (1980); Mukhopadhayay et al. (1981 and 1983); Habib-ur-Rehman (1987); Qureshi (1991)
Stemmadenine	$C_{21}H_{26}N_2O_3$	354	Lf	Mariee et al. (1988); Qureshi (1991)
Strictalamine	$C_{19}H_{20}N_2O$	292	Lf	Habib-UR- Rehman (1987); Qureshi (1991); Fatima (1980)
Strictamine	$C_{20}H_{22}N_2O_2$	322	Lf	Habib -UR –Rehman (1987); Qureshi (1991); Fatima (1980)
Strictamine-N-oxide	$C_{20}H_{22}N_2O_3$	338	Lf	Khanum (1986); Habib -UR –Rehman (1987); Qureshi (1991)
Strictanine	$C_{20}H_{26}N_2O_2$	326	Lf	Habib UR Rehman (1987); Qureshi (1991)
Strictibine	$C_{13}H_{11}NO_2$	213	Lf	Habib-ur-Rehman and Atta-ur-Rahman (1996)
Stricticine	$C_{20}H_{22}N_2O_3$	338	Lf	Habib UR- Rehman (1987); Qureshi (1991); Fatima (1980); Ahmad et al. (1983)
Strictigine	$C_{19}H_{22}N$	278	Lf,Rt	Habib -UR –Rehman (1987); Atta-ur-rahman et al. (1996)
Strictimine	$C_{15}H_{28}N_2O$	252	Lf	Habib -UR –Rehman (1987)
Strictimidine	$C_{19}H_{24}N_2O$	296	Lf	Habib -UR –Rehman (1987); Qureshi (1991)
Strictine	$C_{20}H_{20}N_2O_3$	336	Lf	Ahmad et al.(1983) Habib -UR –Rehman (1987); Qureshi (1991); Fatima (1980)
Strictisidine	$C_{21}H_{22}N_2O_3$	350	Lf	Khanum (1986); Qureshi (1991)
Strictosamide	$C_{26}H_{30}N_2O_8$	498	Lf	Habib- UR –Rehman (1987)
Strictosidine	$C_{27}H_{34}N_2O_9$	530	Lf	Habib- UR- Rehman (1987); Qureshi (1991); Fatima (1980)
(Isovincoside)				
Tabersonine	$C_{21}H_{24}N_2O_2$	336	Lf	Habib- UR –Rehman (1987)
Tetrahydroalstonine	$C_{21}H_{24}N_2O_3$	352	Lf	Habib –UR- Rehman (1987); Qureshi (1991)
Tetrahydropresecamine	$C_{42}H_{56}N_4O_4$	680	Lf	Habib -UR –Rehman (1987); Qureshi (1991); Fatima (1980)
Tetrahydrosecamine	$C_{42}H_{56}N_4O_4$	680	Lf, Rt	Habib -UR –Rehman (1987); Qureshi (1991); Fatima (1980); Bashir et al. (1994)
Tetrahydrosecodine	$C_{21}H_{30}N_2O_2$	342	Lf	Habib -UR- Rehman (1987); Qureshi (1991); Fatima (1980)
Vallesiachotamine,	$C_{21}H_{22}N_2O_3$	350	Lf, Rt	Mukhopadhayay et al.(1981 and 1983); Habib- UR- Rehman (1987); Qureshi (1991)
Vicadine	$C_{21}H_{28}N_2O_2$	340	Lf,Fr	Habib -UR –Rehman (1987); Atta-ur-Rahman and Malik (1985); Qureshi (1991)
(+)-Vincadiformine	$C_{21}H_{26}N_2O_2$	338	Lf	Qureshi (1991); Fatima (1980)
(-)-Vincadiformine	$C_{21}H_{26}N_2O_2$	338	--	Qureshi (1991)
(±)-Vincadiformine	$C_{21}H_{26}N_2O_2$	338	--	Qureshi (1991)
Vincanicine (Deacetylakuammidine)	$C_{20}H_{22}N_2O_2$	322	--	Qures hi (1991)
HR-I	$C_{21}H_{26}N_2O_4$	370	--	Qureshi (1991)

Table 1. Contd.

Non-alkaloidal constituents				
Enzymes				
NADP dependant tetrahydroalstnine cell suspension culture	--	--	--	Zaman (1990)
Strictosidine sythose cell suspension culture	--	--	--	Zaman (1990)
Flavonoids				
Rhazianoside A	$C_{34}H_{42}O_{21}$		--	Zaman (1990)
Rhazianoside B	$C_{34}H_{42}O_{21}\cdot 3H_2O$		--	Zaman (1990)
Glycosides				
isorhamnetin 3-(2,6-dirhamnosylgalactoside)-7- rhamnoside	----------	------	Lf	Zaman (1990)
3-(6-dirhamnosylgalactside)-7- rhamnoside	----------	------	Lf	Zaman (1990)
Peptides				
Phytochelatins	**----------**	**-----**	**--**	Zaman (1990)
Triterpenes				
b-Sitosterol	$C_{29}H_{50}O$	414	Rt	Zaman (1990)
Mg quinate	----------	-----	Rt	Zaman (1990)
Ursolic acid	$C_{30}H_{48}O_3$	456	Rt	Zaman (1990)
3a-hydroxy-ursane-5-ene	$C_{30}H_{50}O$	426	Fr	Sultanaa and Khalid (2010)
stigma sterol	$C_{29}H_{48}O$	412	Fr	Sultanaa and Khalid (2010)
Fatty esters				
9-octadecenoic acid, 20 ,30-dihydroxy propyl ester	----------	-----	--	Sultanaa and Khalid (2010)
Hexadecanoic acid-20 ,30-dihydroxypropyl ester	----------	-----	--	Sultanaa and Khalid (2010)
5, 7-dihydroxy-6, 20-dimethoxy isoflavone	----------	-----	--	Sultanaa and Khalid (2010)
Oleanolic acid	$C_{30}H_{48}O_3$	456	--	Sultanaa and Khalid (2010)

activities in antinociceptive tests (Ali et al., 1995). The opioid antagonist naloxone was ineffective in antagonizing the analgesic effect of *R. stricta*, possibly indicating that this effect occurs via non-opiate pathways. The effect was also suggested to be due to the parent (original) compounds present in the extract, and not to a metabolite thereof. In addition to antinociception, the leaf extract also produced dose-dependent sedation, decreased motor activity, and impaired motor control. The time spent on a rota-rod treadmill was significantly decreased after treatment with the extract. The degree of sedation produced by the extract (8 g/kg, p.o.) was comparable to that produced by diazepam (5 to 10 mg/kg, p.o.). Oral administration of *R. stricta* extract potentiated pentobarbitone sleeping time in a dose-dependent fashion, but did not antagonize picrotoxin-induced

Table 2. Medicinal uses of various parts of *R. stricta.*

Diseases	Part used	Treatment	Reference
Antiinflammatory	W	It is commonly used in the UAE as an antiinflammatory	Tanira et al. (1996)
Antipyretic	Lf	Dhofar is a region in southern Oman that is famous for its green and lush vegetation. In this region, the leaves of *R. stricta* are cooked in water, which is then administered to patients as an antipyretic	Miller and Morris (1988)
Diabetes	W	Arabian communities use *R. stricta* to cure diabetes, inflammatory conditions, and helminthiasis	El-Ghonemi (1993); Tanira et al. (1996)
	W	*R. stricta* is used in traditional medicine for the treatment of diabetes mellitus in UAE	Tanira et al. (1996)
Foot burning	Lf	Fresh leaves are kept in shoes and put under feet for foot burning.	Sultana et al. (2006)
Heat effects.	Sd	Seeds are soaked in the water for a night, and then cooked, a thick liquid is obtained and used for achenes and the removal of the heat effects This paste is used with butter.	Qureshi et al. (2007)
Helminthiasis	W	In Saudi Arabia *R. stricta* is used for the treatment of helminthiasis in camels.	Tanira et al. (1996); Abbas et al. (2002)
Pimples and acne problem of face	Lf	Fresh leaves are dried, crushed and powder is taken with water for pimples and acne problem of face	Sultana et al. (2006)
Rheumatism	W	In the indigenous system of medicine, it is used for the treatment of chronic rheumatism, sore throat and general debility	Chopra et al. (1956)
Skin diseases	Fr,Lf	In the Thar Desert, the fruits and leaves of R. stricta are used as a tonic to cure sore throat and skin diseases	Ahmad et al. (2004)
	W	R. stricta is used in traditional medicine for the treatment of skin infections in UAE.	Bashir et al. (1994)
Stomach pain, colic	W	R. stricta is used in traditional medicine for the treatment of stomach disorders in UAE.	Bashir et al. (1994)
Syphilis	Lf	In the rural areas of Saudi Arabia, the leaves of R. stricta are used in folk medicine as a reputed bitter tonic and a curative for syphilis	Adam (1998)
Tooth ache	St	Branches are used as toothbrush for tooth ache	Sultana et al. (2006)
Tumour	Lf	In India the leaf of the plant is used to treat tumors.	Jewers et al. (1980)
Urinary tract	W	In Unani medicines, R. stricta is used to cure urinary tract disease	Hassan (2006)
Vermifuge	Lf	In Saudi Arabia, the leaves of R. stricta are used as a vermifuge and purgative as well as a treatment for mange.	Al-Yahia et al. (1990)
Wounds	W	In Iran R. stricta is used to cure wounds.	Khaksari et al. (2000)

Key: Fr = fruit, Lf = leaves, Rt = roots, Sd = seeds, W = whole plant.

Table 3. Biological activities of various chemical constituents of *R. stricta.*

Organism	Constituents	References
Antimicrobial activity		
B. subtilis,	Tetrahydrosecamine	Bashir et al. (1994)
E. coli	Strictanol, strictigine, Dihydrocorynantheol, rhazimol, stemmadenine	Bashir et al. (1994); Zaman (1990)
P. aeruginosa,	Tetrahydrosecamine strictanol	Zaman (1990)
Herbicidal activity		
C. pipiens L	Aqueous extracts	Al-Doghairi and Elhag (2002); El-Hag et al. (1996)
A. aegypti	Crude extract	Zaman (1990)
Antifungal activity		
A. flavus	Tetrahydrosecamine	Zaman (1990)
A. flavus,	Chloroform extract	Khan and Khan (2007)
A. fumigatus	Tetrahydrosecamine	Zaman (1990)
A. terreus,	Tetrahydrosecamine	
B. subtilis	Tetrahydrosecamine, Dihydrocorynantheol	Zaman (1990)
C. tropicalis	Akuammidine	Zaman (1990)
T. rubrum	Tetrahydrosecamine	Zaman (1990)
S. fecalis	Akuammidine	Zaman (1990)
M. morginii	Akuammidine	Zaman (1990)
S. aureus	Tetrahydrosecamine, Dihydrocorynantheol	Zaman (1990)
T. longifusis,	Methanol extract	Khan and Khan (2007)
C. albican	Methanol extract	Khan and Khan (2007)
F. solani	Methanol extract	Khan and Khan (2007)
T. longifusis,	Chloroform extract	Khan and Khan (2007)
C. albicans.	Tetrahydrosecamine,stemmadenine	Zaman (1990)
C. albican	Chloroform extract	Khan and Khan (2007)
F. solani	Chloroform extract	Khan and Khan (2007)

convulsions. The extract (4 and 8 g/kg, p.o.) significantly decreased the rectal temperature of normothermic and hyperthermic mice. Oral pretreatment with *R. stricta* (8 g/kg) completely prevented the occurrence of aggressive behaviour in male mice. From the above observations, it was concluded that *R. stricta* has CNS depressant properties (Ali et al., 1995). It has also been suggested that the CNS depressing properties of *R. stricta* may be related to the presence of a b-carboline ring in some constituents (Bashir et al., 1994; Ali et al., 1995). Some b-carbolines are known to possess some of the properties of benzodiazepine agonists (Turski and Stephens, 1993).

Effect on the concentrations of amino acids

In one neurochemical study, the effect of various doses (0.2 to 8 g/kg, p.o.) of the lyophilized leaf extract of *R. stricta* on the concentrations of several inhibitory and stimulatory amino acids was investigated in different brain regions in mice (Ali et al., 2000a). The results indicated that there was no clear or significant effect on the concentrations of these amino acids. Catecholamine and serotonin were also measured in different parts of the brain of rats treated with a single oral dose of a strongly alkaloidal fraction of *R. stricta* leaf extract (250 mg/kg).This treatment produced a significant reduction in the concentration of adrenaline (Tanira et al., 1999).

Effect on arachidonic acid (AA) metabolism

In one report, Saeed et al. (1993) described the effect of an alkaloid isolated from *R. stricta* leaves (rhazimine) on AA metabolism in human blood. The alkaloid has been

shown to be a dual and selective inhibitor of platelet activating factor (PAF)-induced platelet aggregation and AA metabolism *in vitro*. It was concluded that these effects might provide additional beneficial antiinflammatory and anti-PAF effects by comparison with classical nonsteroidal antiinflammatory drugs. These observations are in line with previous results (Tanira et al., 1996) in which lyophilized and butanol extracts of *R. stricta* were found to significantly reduce carrageenan-induced inflammation in the rat paw oedema test, and decrease rectal temperature of pyrexic rats. Activity-guided fractionation indicated that the butanol fraction of *R. stricta* extract was responsible for the anti inflammatory action (Tanira et al., 1996). On a dose-to-dose basis, the potency of the plant fraction was about one tenth of the standard anti-inflammatory drug phenylbutazone (Ali et al., 2000b).

Effect on blood pressure

The lyophilized extract of *R. stricta* (5 to 100 mg/kg, i.v.) caused an inconsistent effect on heart rate, and a dose-dependent decrease in mean blood pressure (MBP) of urethane-anaesthetized rats. The maximum reduction amounted to 40% (Tanira et al., 1996). The alkaloidal fraction was found to be the most effective in this action. It was suggested that using preparations such as frank pithed rat, and spinalized rats, it was suggested that the extract acts centrally, rather than peripherally, to reduce blood pressure. More recently, the alkaloidal fraction was injected into the cerebral ventricles (i.c.v.), and results were similar to those obtained from the i.v. injection (Tanira et al., 2000).

Effect on immunity

In one experiment the possibility that some of the claimed therapeutic actions of the plant extract may be due to immuno-modulatory capacity was tested investigating *ex vivo* production of peritoneal macrophage-derived cytokines in mice. Each mouse received an alkaloidal fraction of *R. stricta* (0.5 and 1.0 mg/animal, i.m. twice weekly for 5 weeks). Peritoneal cells were isolated, cultured and assayed for IL-1a and TNFa using an enzyme-linked immunosorbent assay (ELISA) technique. The alkaloidal fraction of *R. stricta* significantly increased the production of these two proinflammatory cytokines (Tanira et al., 1998).

Effects on serum lipid profile concentrations

The beneficial effects of oral administration of extracts of the *R. stricta* leaves on serum lipid profile concentrations of male Wistar rats were evaluated. Animals of three groups were given a daily single oral dose of 0.5 ml of distilled water containing 0.1, 0.125 and 0.150 gm/ml of the *R. stricta* leaf aqueous extract, respectively for 18 weeks. The blood samples collected, (after an overnight fast, 1, 2, 4, 8, 12 and 18 weeks post-treatment) showed that aqueous extract of the *R. stricta* leaves significantly decreased concentrations of TGs, LDL-c, cholesterol, uric acid and creatinin, but increased concentration of HDL-c. It triggered all these activities without affecting liver enzyme activities or kidney functions. These findings may have a positive impact on the cardiovascular patients and may provide a new therapeutic strategy to reduce hypertriglyceridemia (Baeshin et al., 2009).

Effect on smooth muscles

It was investigated that the lyophilized extract of *R. stricta* has the properties to relax isolated intestinal muscles of rats (Tanira et al., 1996b). Comparison with other medicinal plants of the UAE revealed that *R. stricta* had the highest activity in relaxing the smooth muscles, suggesting that the plant may have potential as an antispasmodic drug. This seems to confirm the folk medicinal use of the plant in certain localities (Ali et al., 2000b).

Diabetic activity

The leaves of *R. stricta* have been used among other ailments, for the treatment of diabetes mellitus (Western, 1989; Gonemi, 1992). The claimed beneficial effect of *R. stricta* in diabetes has been experimentally tested by oral administration of the decoction to streptozotocin-induced diabetic rats under different conditions (Wasfi et al., 1994). The results of this experiment showed no significant improvement in glucose homoeostasis. In another experiment, Tanira et al. (1996a) gave *R. stricta* leaf extract (0.5 to 2 g/kg, p.o.) to streptozotocin-diabetic rats subchronically for 28 days, and found no significant effect on either plasma glucose or insulin concentrations. Conversely, acute oral treatment with the extract at a dose of 4 g/kg produced a significant and short-lived increase in plasma insulin concentration, accompanied by a significant reduction in plasma glucose concentration. In diabetic rats loaded orally with glucose (1 g/kg), *R. stricta* given orally at a dose of 8 g/kg produced significant decreases (16 to 32%) in plasma glucose concentration, at 0.5 and 1 h following the treatment. The plant extract did not significantly affect plasma glucose concentrations in control non-diabetic rats (Tanira et al., 1996).In one study it was found that oral doses of the leaf extract (0.5, 2 and 4 g/kg) reduced the plasma glucose and increased insulin levels at 1 and 2 h following administration to streptozotocin-treated rats. Concomitant oral treatment of diabetic rats with *R. stricta* extract (0.5,

2 and 4 g/kg) and the oral hypoglycaemic drug glibenclamide (2.5, 5 and 10 mg/kg) resulted in exacerbation of the effect on glucose and insulin concentrations caused either by the extract or glibenclamide when given separately. These results seem to imply that co-administration of the extract with oral hypoglycaemic drugs might adversely interfere with glycaemic control in diabetic subjects. This concurs with the previously mentioned clinical observation seen in diabetic clinics in the Arabian Gulf region (Ali et al., 2000b).

Endogenous monoamine oxidase (MAO) A and B inhibitory activity

R. stricta leaves, which have both antidepressant and sedative properties in animal models, are widely used in folk medicine in the Arabian Peninsula. In the study, the effects of oral administration of leaf extracts on rat brain tribulin levels were determined. In an acute study, low doses brought about an increase in MAO A inhibitory activity, while intermediate doses caused a significant reduction. The highest doses had no significant effects on activity. There were no significant effects on MAO B inhibitory activity at any dose. Subchronic administration (21 days) caused a significant decrease in MAO A inhibitory activity, most prominent at low dosage, and an increase in MAO B inhibitory activity. Acute intramuscular administration also resulted in a similar pattern. Such paradoxical effects were at least partially explained when different extracts of the leaves were used; a weakly basic chloroform fraction caused an increase in MAO A inhibitory activity, whereas butanol extracts brought about a decrease. These fractions had no significant effects on MAO B inhibitory activity. These findings show that *R. stricta* leaves contain at least two different components that affect MAO inhibitory activity in opposite directions. It may be that the antidepressant and sedative actions of the plant are explicable in terms of these different components (Ali et al., 1998).

Herbicidal activity

The herbicidal activity of the alkaloidal constituents of *R. stricta* was studied on wild radish (*Raphanus sativus*), Italian ryegrass (*Lolium multiflorum*), lucerne (*Medicago sativa*) and wheat (*Triticum aestivum*). The results show that *R. stricta* has the ability to inhibit the growth of wild radish, a common weed, without affecting the early seedling growth of major crops such as wheat and lucerne (Kamel and Al-Mutlaq, 2004).

Larvicidal effect

The crude extracts of *R. stricta* exhibited larvicidal effects and growth inhibition properties against the fourth instar larvae of *Aedes aegypyti* (Zaman, 1990). Toxicity of the aqueous extracts of *R. stricta* Decne, leaves against larvae of *Culex pipiens* L. was investigated by incurporating the extracts into egg and larval rearing media. Acute LC_{50} was 270 ppm for *R. stricta*. The chronic toxicities for *R. stricta* at concentrations 0.02 and 0.04%, reached 70 and 100% larval mortality, respectively. It conferred significantly reduced larval development and thus, consequently reducing pupation and adult emergence. Only 10 and 33.3% of the larvae reared in media containing 0.02% of *R. stricta* water extract and 0.025% of *Cyanea procera* completed development to the pupa stage. None of the larvae in *R. stricta* extract reached adulthood. Application of *R. stricta* and *C. procera* extracts applied to mosquito larval breeding sites may well provide an environmentally safe method for control of mosquito populations (Al-Doghairi and Elhag, 2002).

Hypotensive activity

(+)-Vincadifformine, an active component has shown hypotensive activity. A dose of 2 mg/kg had the same effect in anesthetised cats as 1mg/kg rserpine while (-) vincadifformine exhibited no hypotensive effect in anesthetised cats (Zaman, 1990).

Leucopenic effect

Extracts of *R. stricta* showed a marked leucopenic effect in rats when given orally (20 mg/kg) and a single intraperitoneal injection (15 mg/kg) significantly reduced the white blood cell count for 7 to 10 days (Zaman, 1990).

Nematicidal activity

R. stricta extracts was also found to provide nematicidal activity at a rate of 100 ppm against nematode *Meloidogyne javanica* (AL-Rajhi et al., 1997).

Oncolytic activity

Siddiqui and coworkers isolated sewarine from the leaves of the *R. stricta* which was found to posses significant oncolytic activity (Zaman, 1990).

Pesticidal activity

R. stricta components were found to have an effect on some agricultural pest. In one study, leaves extract of *R. stricta* affected the growth and caused mortality to Mosquitoes *Culex pipiens* when applied with

concentration range from 100 to 500 ppm, (El-Hag et al., 1996).

CONCLUSION

The extracts of *R. stricta* have significant ambulatory, antifungal, antimicrobial, antioxidant, anti depressant and herbicidal activities. They also showed effects on arachidonic acid (AA) metabolism, blood pressure, central nervous system (CNS), immunity, smooth muscles and glucose homeostasis. *R. stricta* has also been used in traditional medicine against diabetes, foot burning, heat effects, pimples and acne problem of face, rheumatism, skin diseases, stomach pain, colic, syphilis, tooth ache, tumor, urinary tract diseases, vermifuge, and wounds, but still more work needs to be done regarding its medicinal importance (recording and exploring recipes) for the benefit of improving human health, while protecting intellectual property rights (IPR) and following the guidelines of the world health organization (WHO) for safety and efficacy.

A literature review on *R. stricta* also revealed that it has immense potential as an anti-microbial due to its richness of phytochemicals it possesses. In addition to these, research on other aspects such as ecology, taxonomy, conservation, have yet to be conducted. Therefore, such studies are recommended in various parts of the countries of Arabian Peninsula and the Indian subcontinent where it grows.

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