

Review

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

Sarfraz Khan Marwat¹, Fazal-ur-Rehman², Khalid Usman³, Syed Salim Shah⁴, Naveed Anwar⁵ and Imdad Ullah³

¹University WENSAM College Gomal University, Dera Ismail Khan, Pakistan.

²Faculty of Pharmacy, Gomal University, Dera Ismail Khan, Pakistan.

³Faculty of Agriculture, Gomal University, Dera Ismail Khan, Pakistan.

⁴Department of Agriculture, Palosa Campus, Abdal Wali Khan University, Mardan, Pakistan.

⁵Rifah Institute of Pharmaceutical Sciences, Islamabad, Pakistan.

Accepted 29 December, 2011

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).

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).

Description

R. stricta is a small glabrous, erect under shrub or shrub

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).

*Corresponding author. E-mail: skhan.marwat@gmail.com.

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-Rahman, 1996; Mariee et al., 1988; Mukhopadhyay et al., 1981; Mukhopadhyay 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 aches 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 antimicrobial 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, lipoxigenase 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 aureus*, *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=tljp131451446481208&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 petroleum ether, carbon tetrachloride, 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 showed 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 lipoyxygenase 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 ₂ O ₃ | 352 | Lf | Bashir et al. (1994); Fatima (1980); Zaman (1990) |
| Alkaloid R ₁ | C ₂₁ H ₂₄ N ₂ O ₃ | 352 | Lf | Qureshi (1991); Zaman (1990) |
| Alkaloid R ₂ | C ₂₁ H ₂₂ N ₂ O ₃ | 350 | Lf | Habib -UR -Rehman (1987); Qureshi (1991) |
| Alkaloid R ₃ | C ₂₁ H ₂₂ N ₂ O ₃ | 350 | Lf | Habib -UR -Rehman (1987); Qureshi (1991) |
| Antirhine | C ₁₉ H ₂₄ N ₂ O | 296 | Lf | Habib-UR- Rehman (1987); Qureshi (1991); Banerji et al. (1970); Zaman (1990) |
| 3-epi- Antirhine | C ₁₉ H ₂₄ N ₂ O | 296 | Lf | Habib- UR- Rehman (1987) |
| Aspidospermiose | C ₂₄ H ₃₂ N ₂ O ₅ | 428 | Lf | Habib-ur-Rehman and Atta-ur-Rahman (1996) |
| Aspidospermidine | C ₁₉ H ₂₆ N ₂ | 282 | Lf | Habib- UR- Rehman (1987); Fatima (1980) |
| Bhimberine-N-oxide | C ₂₁ H ₂₆ N ₂ O ₄ | 370 | | Qureshi (1991) |
| Bhimberine | C ₂₁ H ₂₆ N ₂ O ₃ | 354 | | Qureshi (1991) |
| Bis-strictidine | C ₃₈ H ₄₈ N ₄ | 556 | Lf | Habib-UR- Rehman (1987); Qureshi (1991) |
| Condyllocarpine | C ₂₀ H ₂₂ N ₂ O ₂ | 322 | Fr | Qureshi (1991) |
| 16S, 16'-Decarboxytetra-hydrosecamine | C ₄₀ H ₅₄ N ₄ O 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 ₂ O | 296 | Lf, Rt | Habib- UR- Rehman (1987) Atta-ur-Rahman and Zaman (1984,1986) |
| 3, 14-Dehydrorhazigine | C ₄₀ H ₄₈ N ₄ O ₂ | 616 | Lf | Habib-UR- Rehman (1987); Qureshi (1991) |
| Didemethoxycarbonyl-1-Carboxymethoxy-b-carboline | C ₁₃ H ₁₀ N ₂ O ₃ | 226 | Lf | Habib-ur-Rehman and Atta-ur-Rahman (1996) |
| Dihydrocorynantheol | C ₁₉ H ₂₆ N ₂ O | 298 | Lf | Habib -UR- Rehman (1987); Qureshi (1991) |
| Dihydroebumamenine | C ₁₉ H ₂₄ N ₂ | 280 | -- | Qureshi (1991) |
| Dihydropresecamine | C ₄₂ H ₅₄ N ₄ O ₄ | 678 | Lf | Habib- UR -Rehman (1987); Qureshi (1991) |
| Dihydrosecamine | C ₄₂ H ₅₄ N ₄ O ₄ | 678 | Lf | Habib -UR -Rehman (1987);Qureshi (1991); Fatima (1980) |
| Dihydrosecodine | C ₂₁ H ₂₈ N ₂ O 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) |
| Ebumamine(pleiocarpinidine) | C ₁₉ H ₂₄ N ₂ O | 296 | Lf | Habib- UR -Rehman (1987); Qureshi (1991); Fatima (1980) |
| Ebumamonine | C ₁₉ H ₂₂ N ₂ O | 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- <i>Epi</i> -Z-isositsirikine | $C_{21}H_{26}N_2O_3$ | 354 | Lf | Mukhopadhyay 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); Mukhopadhyay 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 | Mukhopadhyay 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 tetrahydroalstine 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-dirhamnosylgalactoside)-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 <i>R. stricta</i> are cooked in water, which is then administered to patients as an antipyretic | Miller and Morris (1988) |
| Diabetes | W | Arabian communities use <i>R. stricta</i> to cure diabetes, inflammatory conditions, and helminthiasis | El-Ghonemi (1993); Tanira et al. (1996) |
| | W | <i>R. stricta</i> 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 <i>R. stricta</i> 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 <i>R. stricta</i> are used as a tonic to cure sore throat and skin diseases | Ahmad et al. (2004) |
| | W | <i>R. stricta</i> is used in traditional medicine for the treatment of skin infections in UAE. | Bashir et al. (1994) |
| Stomach pain, colic | W | <i>R. stricta</i> 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 <i>R. stricta</i> 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, <i>R. stricta</i> is used to cure urinary tract disease | Hassan (2006) |
| Vermifuge | Lf | In Saudi Arabia, the leaves of <i>R. stricta</i> are used as a vermifuge and purgative as well as a treatment for mange. | Al-Yahia et al. (1990) |
| Wounds | W | In Iran <i>R. stricta</i> 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 | | |
| <i>B. subtilis</i> , | Tetrahydrosecamine | Bashir et al. (1994) |
| <i>E. coli</i> | Strictanol, strictigine, Dihydrocorynantheol, rhazimol, stemmadenine | Bashir et al. (1994); Zaman (1990) |
| <i>P. aeruginosa</i> , | Tetrahydrosecamine strictanol | Zaman (1990) |
| Herbicidal activity | | |
| <i>C. pipiens</i> L | Aqueous extracts | Al-Doghairi and Elhag (2002); El-Hag et al. (1996) |
| <i>A. aegypti</i> | Crude extract | Zaman (1990) |
| Antifungal activity | | |
| <i>A. flavus</i> | Tetrahydrosecamine | Zaman (1990) |
| <i>A. flavus</i> , | Chloroform extract | Khan and Khan (2007) |
| <i>A. fumigatus</i> | Tetrahydrosecamine | Zaman (1990) |
| <i>A. terreus</i> , | Tetrahydrosecamine | |
| <i>B. subtilis</i> | Tetrahydrosecamine, Dihydrocorynantheol | Zaman (1990) |
| <i>C. tropicalis</i> | Akuammidine | Zaman (1990) |
| <i>T. rubrum</i> | Tetrahydrosecamine | Zaman (1990) |
| <i>S. fecalis</i> | Akuammidine | Zaman (1990) |
| <i>M. morginii</i> | Akuammidine | Zaman (1990) |
| <i>S. aureus</i> | Tetrahydrosecamine, Dihydrocorynantheol | Zaman (1990) |
| <i>T. longifusis</i> , | Methanol extract | Khan and Khan (2007) |
| <i>C. albican</i> | Methanol extract | Khan and Khan (2007) |
| <i>F. solani</i> | Methanol extract | Khan and Khan (2007) |
| <i>T. longifusis</i> , | Chloroform extract | Khan and Khan (2007) |
| <i>C. albicans</i> . | Tetrahydrosecamine, stemmadenine | Zaman (1990) |
| <i>C. albican</i> | Chloroform extract | Khan and Khan (2007) |
| <i>F. solani</i> | 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 homeostasis. 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 aegypti* (Zaman, 1990). Toxicity of the aqueous extracts of *R. stricta* Decne, leaves against larvae of *Culex pipiens* L. was investigated by incorporating the extracts into egg and larval rearing media. Acute LC₅₀ 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 procerca* completed development to the pupa stage. None of the larvae in *R. stricta* extract reached adulthood. Application of *R. stricta* and *C. procerca* 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 anaesthetised cats as 1mg/kg reserpine while (-) vincadifformine exhibited no hypotensive effect in anaesthetised 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 possess 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.

REFERENCES

- Adam SEI (1998). Toxicity of *Rhazya stricta* to sheep. *Vet. Human Toxicol.*, 40: 68-69.
- Ahmad H, Bhati GR, Latif A (2004). Medicinal flora of the Thar Desert: An overview of problems and their feasible solutions. *Zonas Aridas*, 8: 1-11.
- Ahmad Y, Fatima K, Le Quesne PPW, Atta-ur-Rahman (1983). Further alkaloidal constituents of the leaves of *Rhazya stricta*. *Phytochemistry*, 22: 1017-1019
- Al Gonemi AA (1992). *Encyclopaedia of the United Arab Emirates Plants Used in Folk Medicine*, United Arab Emirates University Press: Al-Ain, (in Arabic), pp. 345-346.
- Ali BH, (2002). The effect of treatment with the medicinal plant *Rhazya stricta* decne on gentamicin nephrotoxicity in rats. *Phytomedicine*. 9(5): 385-9.
- Ali BH, Alqarawi AA, Bashir AK, Tanira MO (2000a). Antioxidant Action of Extract of the Traditional Medicinal Plant *Rhazya stricta* Decne. in Rats, *Phytother. Res.*, 14: 469-471.
- Ali BH, Al-Qarawi AA, Bashir AK, Tanira MO (2000b). *Phytochemistry, Pharmacology, and Toxicity of Rhazya Stricta* Decne: A Review. *Phytother. Res.*, 14: 229-234
- Ali BH, Bashir AK, Banna NR, Tanira MOM (1995). Central Nervous System Activity of *Rhazya stricta* Decne in Mice. *Clinical and Experimental Pharmacology and Physiology (CEPP)*, pp. 22 (4): 248-253 Article first published online: 28 JUN 2007
- Ali BH, Bashir AK, Tanira MOM (1999). The Effect of *Rhazya stricta* Decne, a Traditional Medicinal Plant, on Spontaneous and Drug-Induced Alterations in Activity of Rats. *Pharmacol. Biochem Behav.*, 64(3): 455-459
- Ali BH, Bashir AK, Tanira MOM, Medvedev AE, Jarrett N, Sandler M, Glovr V (1998). Effect of extract of *Rhazya stricta*, a traditional medicinal plant, on rat brain tribulin. *Pharmacol. Biochem. Behav.*, 59(3):671-675.
- Al-Rajhi DH, Al-Hazmi AS, Hussein HI, Ibrahim AAM, Al-yahya FA, Mostafa S (1997). Nematocidal Properties of *Rhazya stricta* and *Juniperus polycarpus* on *Medoidogyne javanica* in Saudi Arabia. *Alex. Sci. Exch.*, 18:135-142.
- Al-Yahya MA, Al-Meshal IA, Mossa JS, Al-Badr AA, Tariq M (1990). *Saudi Plants: A Phytochemical and Biological approach*. King Saud University Press, Riyadh. pp. 123-129
- Al-Doghairi MA, Elhag EA (2002). Effect of *Rhazya stricta*, *Calotropis procera*, and *Francoeuria crispa* on Larvae and Eggs of *Culex pipiens*. *J. Her. Spic Med. Pl.*, 10(2):25-33
- Atta-ur-rahman, Zaman K, Khanum S, Muzaffar A, Badar Y, Fatima K (1996). Strictigine - A Novel 4-Vinylquinoline Alkaloid from *Rhazya stricta*. *Nat. Prod. R.*, 8(1): 55 - 66
- Atta-ur-Rahman, Khanum S (1985). 2-Methoxy-1,2-dihydrohazimine, an alkaloid from the leaves of *Rhazya stricta*. *Phytochemistry*, 24: 1625-1626.
- Atta-ur-Rahman, Khanum S, Badar Y, Fatima K, Ahmad Y (1987). N-Methyl strictamine a new alkaloid from the leaves of *Rhazya stricta*. *Z. Naturforsch.*, 42b: 91-93.
- Atta-ur-Rahman, Malik S (1985). Vincadine from the legumes of *Rhazya stricta*. *J. Nat. Prod.*, 48: 153-154.
- Atta-ur-Rahman, Zaman K (1986). 1,2-Dehydroaspidospermidine N-oxide, an alkaloid from *Rhazya stricta*. *Phytochemistry*, 25: 1779-1780.
- Atta-ur-Rahman, Zaman K, Habib-ur-Rehman, Malik S (1986). Studies on alkaloids of *Rhazya stricta*. *J. Nat. Prod.*, 49: 1138-1139.
- Baeshin NA, El-Twaty NH, Al-Hebshi AM (2005). Evaluating the Genotoxicity of *Rhazya stricta* leaves extract by the Saccharomyces cerevisiae auxotrophic mutants test. *Egypt. J. Natur.Tox.*, 2: 87-100.
- Baeshin NA, Lari SA, Al-Doghhaither HA, Elkady AI (2009). Effects of aqueous extracts of *Rhazya stricta* on blood lipid profile concentrations, liver enzyme activities and kidney functions in rats. *J. Appl. Sci. Resear. No. September* pp. 1103-1109
- Banerji A, Majumder PL, Chatterjee A (1970). Occurrence of geissoschizine and other minor biogenetically related alkaloids in *Rhazya stricta*. *Phytochemistry*, 9:194-143.
- Bashir AK, Abdalla AA, Hassan ES, Wasfi IA, Amiri MA, Crabb TA (1994). Alkaloids with antimicrobial activity from the root of *Rhazya stricta* Decn. growing in United Arab Emirates. *A. Gul. J. Sci. Res.*, 12(1): 119-131.
- Batanouny KH, Tabl SA, Shahbana M, Soliman F (1999). *Wild Medicinal Plants in Egypt*. P.7 <http://www.uicnmed.org/nabp/web/documents/book/medpreface.pdf>
- Chopra RN, Nayar SL, Chopra IC (1956). *A Glossary of Indian Medicinal Plants*. CSIR: New Delhi, pp. 212.
- EL-Hag, EA, Harraz FM, Zaytoon AA, Salam AK (1996). Evaluation of Some Wild Herb Extracts for Control of Mosquitoes, (Culicidae, Diptera). *J. King Saud Univ. Agric. Sci.*, 8:135-145.
- Fatima K (1980). Isolation and Structure Elucidation of Alkaloids from "*Rhazya stricta*" (Ph.D Thesis). H.E.J. Research Institute of Chemistry/ University of Karachi, pp.1-123
- Gilani SA, Kikuchi A, Khan ZS, Khattak ZI and Watanabe KN (2007). *Phytochemical, Pharmacological and Ethnobotanical Studies of Rhazya stricta*. *Phytother., Res.*, 21: 301-307
- Habib-Ur-Rehman (1987). Isolation and Structural Studies on the Chemical Constituents of *Rhazya stricta* and Related Medicinal Plants (Ph.D Thesis). University of Karachi/ H.E.J. Res. Inst. Chem., Pp.1-318.
- Habib-ur-Rehman and Atta-ur-ahman (1996). Alkaloids of the leaves of *Rhazya stricta*. *Fitoterapia*, 37: 145-148
- Hassan HM (2006). Use of traditional unani medicine for primary health care. *TelMedPakAgriculture Tuesday*, Available on-line at:http://www.telmedpak.com/agricultures.asp?a=medplantpak&b=med_plant5.
- Iqbal S, Bhangar MI, Akhtar M, Anwar F, Ahmad KR, Anwer T (2006). Antioxidant properties of methanolic extracts from leaves of *Rhazya stricta*. *J. Med. Food*, (2): 270-275.
- Jafri SKH (1966). *The Flora of Karachi*, The Book Corporation, Karachi, pp. 246-247.
- Jewers K, Pusey DFG, Sharma SR, Ahmad Y (1980). 13-C-NMR

- spectral analysis of rhazine, quebrachamine and rhazinilam. *Planta Med.*, 38: 359–362
- Kamel A, Al-Mutlaq K (2004). Selective herbicidal activity of an indole alkaloid isolated from *Rhazya stricta* Decne. growing in Saudi Arabia. Presented in 14th Australian Weeds Conference, Wagga Wagga, New South Wales, Australia, 6-9 September: papers and proceedings, 270-273
<http://www.cabdirect.org/abstracts/20053008430.html>
- Khaksari M, Rezvani ME, Sajadi MA, Soleimani A (2000). The effect of topically applied water extract of *Rhazya stricta* on cutaneous wound healing in rats. *Koomish*, 1(3): 1.
- Khan S, Khan GM (2007). In Vitro Antifungal Activity of *Rhazya stricta* Decne Pak. *J. Pharm. Sci.*, 20(4): 274-279
- Khanum S (1986). Isolation and Structural studies on alkaloids of *Rhazya stricta* and synthetic studies in the field of pyridyl indole, Institute H.E.J. Res. Chem./ Uni. Karachi, Pp.1-133.
- Mariee N, Khalil AA, Nasser AA, Al-Hiti MM, Ali W (1988). Isolation of the antimicrobial alkaloid stemmadenine from Iraqi *Rhazya stricta*. *J. Nat. Prod.*, 51: 186–187.
- Miller AG, Morris M (1988). Plants of Dhofar, the Southern Region of Oman: Traditional, Economic and Medicinal Uses. Conservation of the Environment, Diwan of Royal Court, Sultanate of Oman, pp. 34.
- Mukhopadhyay S, El-Sayed A, Handy GA, Cordell GA (1983). Catharanthus alkaloids XXXVII. 16-Epi-isositsirikine, a monomeric indole alkaloid with antineoplastic activity from *Catharanthus roseus* and *Rhazya stricta*. *J. Nat. Prod.*, 46: 409-413.
- Mukhopadhyay S, Handy GA, Funayama S, Cordell GA (1981). Anticancer indole alkaloids of *Rhazya stricta*. *J. Nat. Prod.*, 44: 696-700.
- Qureshi MM (1991). Isolation and Structural Studies on the Chemical Constituents of *Rhazya stricta*, *Alstonia macrophylla* and Related Medicinal Plants (Ph.D Thesis). University of Karachi/H.E.J. Res. Inst. Chem., pp. 238
- Qureshi RA, Gilani SA, Ghufuran MA (2007). Ethnobotanical Studies of Plants of Mianwali District Punjab, Pakistan. *Pak. J. Bot.*, 39(7): 2285-290.
- Saeed SA, Simjee RU, Mahmood F, Sultana N, Atta-ur-Rahman. (1993). Rhazimine from *Rhazya stricta*: A dual inhibitor of arachidonic acid metabolism and platelet activating factor-induced platelet aggregation. *Planta Med.*, 59: 566–568.
- Sultana N, Khalid A (2010). Phytochemical and enzyme inhibitory studies on indigenous medicinal plant *Rhazya stricta*. *Nat. Prod. Res.*, 24(4):305-314.
- Sultana S, Khan MA, Ahmad M, Zafar M (2006). Indigenous Knowledge of Folk Herbal Medicines by the Women of District Chakwal, Pakis. *Ethnobotanic.Leafl.*, 10: 243-253.
- Tanira MOM, Ali BH, Bashir AK, Chandernath I (1996). Some pharmacological and toxicological studies of *Rhazya stricta* Decne. in rats, mice, and rabbits. *Gen. Pharmacol.*, 27: 1261-1267.
- Tanira MOM, Ali BH, Bashir AK, Dhanasekaran S (1999). The effect of *Rhazya stricta* strongly basic alkaloidal fraction on rat brain catecholamines. *Br. J. Pharmacol.*, 98:567.
- Tanira MOM, Ali BH, Bashir AK, Dhanasekaran S, Tibricia EM, Alves LM (2000). Mechanism of the hypotensive activity of the alkaloidal fraction of *Rhazya stricta*. *Pharmacol. Res.*, 41: 369-378.
- Tanira MOM, Ali BH, Bashir AK, Stephen S, Lukic M (1998). *Rhazya stricta* enhances IL-1 and TNF α production by macrophages in mice. *FASEB J.* pp. 12: A764.
- Turski L, Stephens DN (1993). Effect of the b-carboline abercarnil on spinal reflexes in mice: A comparison with diazepam. *J. Pharmacol. Exp. Ther.*, 267: 1215-1220.
- Wasfi IA, Bashir AK, Amiri MH, Abdalla AA (1994). The effect of *Rhazya stricta* on glucose homeostasis in normal and streptozotocin diabetic rats. *J. Ethnopharmacol.*, 43: 141-147.
- Western AR (1989). *Rhazya stricta* Decne. In: The Flora of the United Arab Emirates, an Introduction. United Arab Emirates University Press: Al-Ain, P. 111.
- Zaman K (1990). Studies on the Chemical Constituents of Roots of *Rhazya stricta* Decne. Institute/University/Department Details University of Karachi/H.E.J. Res. Inst. Chem., Pp. 1-250.