Pharmocological and Biological Activities

The extracts of roots of *R. stricta* exhibited various biological activities, particularly antimicrobial, antimitotic, antifungal and hypotensive activities (Zaman, 1990). (+)-Vincadifformine has shown hypotensive activity. A dose of 2 mg/kg had the same effect in anesthetized cats as 1 mg/kg reserpine (Racz-Kotilla, 1975) while (-) vincadifformine exhibited no hypotensive effect in anesthetised cats (Van Beek *et al*., 1984).

Results obtained by Khan and Khan (2007) studies showed that fractionated samples of methanol and chloroform extracts possessed significant antifungal activities. The extract of *Rhazya stricta* has potent lethal and mutagenic activities in *Saccharomyces cerevisiae* cell culture (Baeshin *et al*., 2005). It was shown that dimeric compounds are much more active than the monomers from which they are derived against some fungi and bacteria. Among the terpenoid indole alkaloid, the secamines were reported to be the most active (Verpoorte *et al*., 1982, 1983).The antimicrobial activities of several isolated alkaloids have been reported e.g. tetrahydrosecamine, rhazimol, stemmadenine, 16-demethoxy-carbonyltetrahydrosecamine, dihydrocorynantheol and akuammidine (Mukhopadhay *et al*., 1981; Mariee *et al*., 1988; Zaman, 1990; Bashir *et al*., 1994b).

The aqueous extract of the *Rhazya stricta* leaves significantly decreased concntrations of TGs, LDL-c, cholesterol, uric acid and creatinin, but increased concentration of HDL-c (Baeshin *et al*., 2009). The extract of *R. stricta* at doses of 0.2 and 0.5/kg significantly ($p < 0.05$-0.01) increased the hepatic and cerebral activity of monoamine oxidase (MAO) in rats by 36-127% (Ali *et al*., 2000b). Rhazimine, isolated from the leaves is an arachidonic acid metabolism inhibitor (Atta-ur-Rahman and Khanum, 1984b; Saeed *et al*., 1993). Ali *et al*. (1998b) reported that the 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*., 1998a,b). Fruit extracts (ethanolic) showed lipoxygenase and acetylcholinesterase activities (Sultana and Khalid, 2010).

Studies on the effect of *Rhazya stricta* extracts revealed that the co-administration of these extracts with oral hypoglycemic drugs may adversely interfere with glycemic control in diabetic subjects (Wasfi *et al*., 1994, 1995; Tanira *et al*., 1996b; Ali, 1997; Ali *et al*., 2000a). *R. stricta* has the potential to interact with other drugs that are biotransformed by cytochrome P450, when given concomitantly with them (El-Kadi *et al*., 2003).

The extracts of *R. stricta* possess several activities *viz.* antioxidant activity (Ali *et al*., 2000c; Iqbal *et al*., 2006), antispasmodic, anti-inflammatory (Wasfi *et al*., 1995; Tanira *et al*., 1996b; Gilani *et al*., 2007), CNS depressant (Marwat *et al*., 2012), hepatoprotective (Ali *et al*., 2001; Gilani *et al*., 2007), immunomodulator (Tanira *et al*., 1998), antispasmodic (Tanira *et al*., 1996b; Gilani *et al*., 2007), antidepressant, sedative (Ali *et al*., 1995 and 1999), lipoxygenase- and acetylcholinesterase-inhibitory (Sultana and Khalid, 2010).

Many alkaloids of *R. stricta* possess antitumor activity (Spiteller, 1963; Cordell, 1981). Sewarine, isolated from the leaves, was found to possess significant oncolytic activity (Marwat *et al.*, 2012). Tetrahydrosecamine and 16-*epi*-*Z*-iso-sitsirikine also displayed antineoplastic activity in the KB test system *in vitro* and p-388 test system *in vivo* (Spitteler, 1963; Atta-ur-Rahman and Malik, 1984a). Vallesiachotamine also showed moderate *in vivo* cytotoxic activity (Mukhopadhyay *et al*., 1981). Rhazimol and tetrahydroalstonine exhibited

antimitotic activity (Gueritte *et al*., 1983). The plant extract and alkaloids from the plant showed a leucopenic effect (Bisset, 1958; Siddiqui and Bukhari, 1972; Atta-ur-Rahman and Khonum, 1984a). The cytotoxicity of the several other alkaloids, isolated from the plant was reported (Mukhopadhyay *et al*., 1983; Pawelka and Stockigt, 1986; Gilani *et al*., 2007).

Neurochemical studies on rats showed that various doses (0.2-8 g/kg) did not significantly affect the concentrations of inhibitory and stimulatory amino acids in brain regions in mice (Ali *et al*., 2000b). An oral dose of a strongly alkaloid fraction of *Rhazya stricta* leaf extract (250 mg/kg) significantly reduced the concentration of adrenaline (Tanira *et al*., 1999). Moreover, an alkaloidal fraction caused a dose-dependent reduction in the mean arterial blood pressure (MAP) of urethane-anesthetized rats. Direct intracerebroventricular injection of the AF (0.1-0.4 mg) also significantly reduced MAP (Tanira *et al*., 2000). The hypotensive action of AF is centrally mediated (Tanira *et al*., 2000) (Gilani *et al*., 2007).

Ali (2002) reported that *R. stricta* water extract may contain compounds that could potentially ameliorate gentamicin nephrotoxicity in rat. A decrease in body weight and feed efficiency and hepatonephropathy were observed in chicks fed on a 100 g/kg *R. stricta* diet (Al-Homidan *et al*., 2002; Gilani *et al*., 2007).

Daily oral dosing of *R. stricta* leaves (0.25 g/kg) for 42 days was not fatal to sheep, but the mixture of *Nerium oleander* with *R. stricta* leaves proved fatal to animals within 24h, with dyspnea, grunting, salivation, grinding of the teeth, ruminal bloating, frequent urination, ataxia and recumbence prior to death (Adam *et al*., 2002). The mixture of *R. stricta* leaves and *Citrullus colocynthis* fruits (0.25g + 0.25 g/kg/day) proved fatal within 26 days in Najdi sheep, which experienced profuse diarrhea, dehydration, decreased condition, ataxia and recumbence prior to death (Adam *et al*., 2000).Toxicity of the plant has been reported (Adam, 1998a,b, 1999). The oral use of 1 g/kg/d caused body weight depression, ruminal bloat, diarrhea, dyspnea and weakness of the hind limbs. Enterohepatonephropathy, pulmonary congestion, hemorrhage and emphysema, lymphocytes in vital organs, and congestion of the blood vessels of the heart were associated with increases in serum AST and LDH, in elevated bilirubin and urea concentrations, and decreased total protein, albumin and calcium concentrations, and leucopenia and anemia (Adam, 1998b). The results obtained by Rasheed *et al*. (1997) are suggestive of potential fetal toxicity of *R. stricta* if taken during pregnancy. Decreased growth rate, soft feces, dullness, ruffled hair and hepatonephrotoxicity were observed in rats on 10% and 50% *R. stricta* diet. Fifty percent *Rhazya* was fatal to rats (Adam, 1999).

Methanol and ether extracts of *Rhazya stricta* showed marked acute chronic toxic effects, respectively, on *Culex pipiens* mosquito larvae (El Hag *et al*., 1999) (Gilani *et al*., 2007). The petroleum ether extract of *R. stricta* has antifeedant and toxic activity against larvae of cotton leafworm (*Spodoptera littoralis*) (Abdel-Rahman and Al-Mozini, 2007). The plant extracts exhibited allelopathic (Gilani *et al.*, 2010b) herbicidal, larvicidal, pesticidal, nematicidal activities (Marwat *et al*., 2012).