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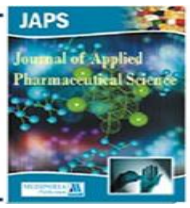

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The study on Morphological, Phytochemical and Pharmacological aspects of *Rhinacanthus nasutus.* (L) Kurz (A Review)

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ABSTRACT

The present review provides an account of the knowledge on the morphology, phytochemistry and pharmacological aspects of *Rhinacanthus nasutus R Kurtz.* This plant also called Nagamalli is a perennial shrub growing to 60-76 cm in height with tender stem. A wide range of chemical compounds have been isolated, mainly flavonoids, benzenoids, coumarin, anthraquinone, quinone, glycosides, carbohydrate, triterpenes, sterols, anthraquinones, napthoquinones. Different parts of plant have been used in folk medicine for treating liver disorders, skin diseases, peptic ulcers, helminthiasis, scurvy, inflammation and obesity. The napthoquinones known as rhinacanthin-C and rhinacanthin-D, extracted from the *R.nasutus* are reported to have anti-inflammatory and analgesic activity. The promising alkaloid, Rhinacanthin isolated from *R.nasutus* having antibacterial and antihelmintic activity. *R.nasutus* shows several other characteristic pharmacological effects like platelet aggregation inhibitor, antidiabetic, antituberculosis, anticancer which are consistent with the reported uses of the plant extracts in the indigenous system of medicine. Further the leaves of this plant are used in the preparation of shampoos or detergents. Hence the present article includes the detailed exploration of morphology, phytochemistry, and pharmacological aspects of *R.nasutus* in an attempt to provide a direction for further research.

Key words: Rhinocanthus, Pharmaceutical uses, medicinal compounds, rhinocanthecins.

INTRODUCTION

Medicinal plants, since times immemorial, have been used in virtually all cultures as a source of medicine. The widespread use of herbal remedies and healthcare preparations, as those described in ancient texts such as Bible and the Vedas, and obtained from commonly used traditional herbs and medicinal plants, has been traced to the occurrence of natural products with medicinal properties. Medicinal plants are staging a comeback and 'renaissance' is happening all over the globe. The Medicinal plants products today symbolise safety in contrast to the synthetics that are regarded as unsafe to human and environment. Green plants synthesize and preserve a variety of biochemical products, many of which are extractable and used as chemical feed stocks or as raw material for various scientific investigations. Many secondary metabolites of plant are commercially important and find use in a number of pharmaceutical compounds (Joy *et al.*, 2001). Although Medicinal plants had been priced for their medicinal qualities for centuries, the synthetic products of the modern age surpassed their importance, for a while. However, the blind dependence on synthetics is over and people are returning to the naturals with hope of safety and security. In recent times, focus on plant research has increased all over the world and a large body

of evidence has collected to show immense potential of medicinal plants used in various traditional systems. More than 13,000 plants have been studied during the last 5 year period (Dahanukar *et al*., 2000). Over three-quarters of the world population relies mainly on plants and plant extracts for health care. Isolated and purified compounds, in contrast, may lose their biological activity or fail to behave in the same way as in the complex matrix that the original item of food represents (Rao *et al*, 1998; Raveendra *et al*, 2008).

The drugs are derived from the whole plant or from different parts like leaves, stem, bark, root, flower, seed, etc. More than 30% of the entire plant species, at one time or other was used for medicinal purposes. It has been estimated that in developed countries such as United States, plant drugs constitute as much as 25% of the total drugs, while in fast developing country such as India; the contribution is as much as 80% (Joy *et al*., 2001). Thus, the economic importance of medicinal plants is much more to countries such as India than to rest of the world.

Rhinacanthus nasutus: Geographical distribution and Ethanomedical uses

The genus *Rhinacanthus* comprises of about 25 species confined to the Old World tropics and subtropics. Within the *Acanthaceae* family, it placed in the *Justiciinae* subtype (Scotland and Vollesen, 2000). *R.nasutus* is widely distributed in some parts of sub-continent, in the region of Southeast Asia and China (Farnsworth and Bunyapraphatsara, 1992). It is typically found wild in the road bushes and is shade loving perennial shrub commonly known as rangchita.

The plant is a small slender shrub, 60-76 cm in height. It requires 1000-1200mm rainfall and 20-28ºC temperature suitable for optimum growth of the plant. During rainy season the plant grows vigorously where as in summer, the aerial part mostly dries up and the root portion remains intact. It is highly susceptible to water logging and water stagnation for period of 1-2 days cause damage to the plant (Nilanjan Das, 2006). The *R.nasutus* (Nagamalle) is cultivated particularly as a medicinal plant has been used in treatments and preventions of diverse diseases as folklore medicines. Different parts of *R.nasutus* have used in traditional medicine for the treatment in diseases such as eczema, pulmonary tuberculosis, herpes, hepatitis, diabetes, hypertension and several skin diseases (Siripong *et al*., 2006). In the some experiments, it has potential effects for treatment of some diseases like to treat cancer, liver disorders, skin diseases, peptic ulcers, helminthiasis, scurvy, inflammation and obesity (Suja *et al*., 2003).

Taxonomy

Kingdom: Plantae – Plants
Division: Magnoliophyta - Flowering plants
Class: Magnoliopsida
Family: Acanthaceae
Subfamily: Acanthoideae
Genus: Rhinacanthus
Species: nasutus - (L.)

Common names

Snake Jasmine, Rangchita Dainty, Spurs, Palakjuhi, Juhipani, Gajkarni, Uragamalli, Nagamalli, Nagamulla, Puzhukkolli, Nagamalle, Nagamallige, Doddapatike, Juipana, Dadmari, Palakjuhi, and Yudhikaparni.

Morphology

The plant is a slender, erect, branched, somewhat hairy shrub 1-2 m in height (Fig 1). The leaves are oblong, 4-10 cm in length, and narrowed and pointed at both ends. The inflorescence is a spreading, leafy, hairy panicle with the flowers usually in clusters. The calyx is green, hairy, and about 5 mm long. The corolla-tube is greenish, slender, cylindric, and about 2 cm long. The flowers is 2-lipped; the upper lip is white, erect, oblong or lancelike, 2-toothed at the apex, and about 3 mm in both length and width; and the lower lip is broadly obovate, 1.1-1.3 cm in both measurements, 3-lobed, and white, with a few, minute, brownish dots near the base. The fruit (capsule) is club-shaped and contains 4 seeds.

Fig 1: Rhinacanthus nasutus (Linn.) Kurz available in Tirumala Hills.

Phytochemistry

Studies on phytochemical of *R.nasutus* species have demonstrated flavonoids, steroids, terpenoids, anthraquinones, lignans and especially naphthoquinone analogues as major constituents

Naphthoquinones viz., rhinacanthins A, B, C, D, G, H, I, J, K, L, M, N, O, P, and Q were isolated and characterized from leaves and roots of *R.nasutus* plant (Wu *et al* 1998 a, b; Sendl *et al* 1996). The rhinacanthone from leaves and stems (Kodama *et al* 1993 and Kuwahara *et al* 1995) and dehydro α-lapachone from roots were also isolated (Wu *et al* 1998a, b).The lignans rhinacanthin –E and -F were isolated from aerial parts (Kernan *et al* 1997). The Benzenoids compounds p-hydroxy-benzaldehde, vanillic acid, syringic acid, 2 methoxy-propionolphenol, methyl valinate and

syringaldehyde were isolated from leaves, roots and stems (Wu *et al* 1995,1998b)

Wu *et al* (1995) isolated anthraquinone compound 1, 2-methyl from leaves and stem. The Triterpeniods compounds β-amyrin, glutinol and lupeol were also derived from roots (Wu *et al* 1995.1998b). Wu *et al*., (1998b) and Subramanian *et al*., (1981) reported wogonin, oroxylin- A, rutin compounds from roots and flowers. The sterols compounds stigmasterol and β-sitosterol from roots (Wu *et al* 1998) and chlorophyll are methylphecophrorbide-A from leaves and stems were also identified (Wu *et al* 1995).

The previous studies reported coumarins (+)-pracruptorin and umbelliferone derived from roots, leaves, stems (Wu *et al* 1998b and 1995) and the benzoquinone compound 2,6-dimethoxy benzoquinone from leaves and stems (Wu *et al* 1995). Various other constituents which have been reported from *R.nasutus* include carbohydrate viz. methyl-α-D-galactopyranoside, quinol compound 4-acctony 1-3,5-dimethoxy-p-quinol and glycosides compounds sitosterol-β-D-glucopyranoside, stigmasterol-β-D-glucopyranoside, 3,4-dimethylphenol--β-D-glucopyranoside, 3,4,5-dimethylphenol--β-D-glucopyranoside were isolated from leaves and stems (Wu *et al* 1995).

Pharmacological aspects of *Rhinacanthus nasutus*

Antifungal activity

It has been reported that *Rhinacanthus nasutus* extract has been evaluated for antifungal activity against different microorganisms such as *Microsporum gypeseum, M. canis, Trichophyton rubrum, T. mentagagrophytes, Epidermophytes floccosum, Candida albicans, Cryptococcus neoformans* and *Saccharomyces spp*. (Farnsworth and Bunyapraphatsara, 1992; Kodama *et al* 1993; Akatsuka *et al*., 2006; Panichayupakaranant *et al*., 2000; Darah and Jain, 2001). Rhinacanthone also has been demonstrated to be antifungal active compound, exhibited by inhibitory action on the spore germination of *Pyricularia oryzae* (Kuwahara *et al*., 1995). Kongchai, (2002) and Panichayupakaranant *et al* (2000 & 2002) investigated the antifungal activity of rhinacanthin-C, D and N of *R.nasutus* leaf extract against *M.gypseum, T.rubrum and T.mentagrophytes, Candida albicans*.

Antifungal activity of the crude extract of *R.nasutus* was also determined against *Aspergillus niger* (Visweswara Rao *et al* 2010). It was found that ethanolic extract of *R.nasutus* exhibited a potent dose dependent antifungal activity against *C. albicans, Trichophyton mentagraphtes* (Abdual *et al* 2004). Rhinacanthin rich *R. nasutus* extract also exhibited antifungal activity against *C.albicans* (Puttarak *et al* 2010)

Antibacterial activity:

Apisariyakul *et al.*, (1991) reported that leaf and stem extracts of *R.nasutus* exhibited inhibitory against oral *Streptococcus spp*. (22 isolated strains). *R.nasutus* leaves extract antibacterial potential against gram positive bacteria such as *Bacillus cereus, Bacillus globigill, Bacillus subtilis* and *Staphylococcus aureus* and gram negative bacteria such as *Proteus morgani, Proteus mirabilis, Salmonella thyphi, Pseudomonas aeruginosa and Escherichia coli* (Sattar *et al* 2004).

The antibacterial activity of extracts of *R.nasutus* was evaluated against clinically isolated bacteria from Thai cancer patients viz., coagulase positive *Staphylococci,* coagulase negative *Staphylococci, Hexolytic Streptococci, Enterococci, E.coli, Klebsiella spp, Enterobacter sp, Pseudomonas aeruginosa* (Siripong *et al* 2006)

Puttarak *et al*. *2010* studied antimicrobial activity of the Rhinacanthins-rich *R.nasutus* extract as well as Rhinacanthin-C against *Streptococcus mutans, Propinibacterium acnes, Helicobacter* pylori, *Staphylococcus aureus Staphylococcus* epidermidis. The ethanolic extract of *R.nasutus* leaves was also exhibited *in vitro* antibacterial activity against human pathogens (Prabhakaran and Pugalvendhan, 2009)

The *in vitro* antibacterial activity of *R.nasutus* leaves was also investigated against various strains *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumonia* (Visweswara Rao *et al*., 2010)

Antiviral activity

Antiviral activity of rhinacanthin-C and D against cytomegalovirus in mice (mCMV) and human (hCMV) influenza viruses type–A, herpes simplex viruses type 2 and respiratory syncytial viruses compared with gancyclovire, amantadine, acyclovir and ribavirin (Sendl *et al* 1996). In addition two new lignans rhinacanthin-E and –F were isolated from the aerial parts of *R. nasutus* showed significant antiviral activity against influenza virus type A (Kernan *et al* 1997).

Cytotoxic activity

The methanol *R.nasutus* extract and rhinacanthin-B isolated from the roots showed significant cytotoxicity against human KB tumor cell (human epidermoid carcinoma) (Wu et al., 1988). The naphthoquinones and flavonoids including rhinacanthin-A, -B, -C, -G, -H, -I -K, -M, -N, -Q, and wogonin, isolated from the root of *R.nasutus* exhibited significant cytotoxic activity against murine leukemia (P-388), human lung carcinoma (A-549), human colon adenocarcinoma (HT-29), and leukemia (HL-60) cells (Wu *et al*., 1998b).

Ethanolic extracts Rhinacanthus nasutus was investigated for cytotoxicity by MTT assay and inhibition of hepatitis B surface antigen secretion from PLC/PRF/5 cells and accounted for their inhibitory activity (Thaveechai *et al.*, 2006). MeOH extracts from aerial part and roots of *R.nasutus* were investigated for cytotoxic activity against human tumor cells and were determined by the MTT method (Haruka *et al*., 2011).

Antitumour activity

The antitumour activity of rhinacanthone against Dalton's ascetic lymphoma (DAL) in mice has been reported (Thirumurugan *et al.*, 2000). A significant enhancement of mean survival time of tumor bearing mice and peritoneal cell count in normal mice was observed with respect to the control group.

Panichayupakaranant and his group had studied antitumor activity of rhinacanthins in *R.nasutus* leaves against HeLa (human cervical carcinoma) and MCF (human Caucasian breast adenocarcinoma) (Panichayupakaranant, 2003). The rhinacanthin -M,-N, and -Q synthesized from esterification of naphthoquinone-3 (propan-3′-ols) with benzoic or naphthoic acids showed significant cytotoxic activity against KB, HeLa (human cervical carcinoma), and HepG2 (human hepatocellular carcinoma) cell lines (Kongkathip *et al*., 2004).

Liposomal Rhinacanthins, showed strong antiproliferative activity against HeLaS3 cells and also these liposomes suppressed the tumor growth in Meth-A sarcoma-bearing BALB/c mice (Siripong *et al*., 2006). Rhinacanthone has chemical structure closely related to β-lapachone (3,4-dihydro-2,2-dimethyl-2H-naphthol[1,2- *b*] pyran-5,6-dione) which was proved to be a novel anticancer drug and DNA topoisomerase I and II inhibitor. Rhinacanthins-N and -Q also act as topoisomerase II inhibitors (Siripong *et al.,* 2009). This *R.nasutus* inhibited the mutagenic responses induced by the product of 1-aminopyrene nitrite model in both strains of Salmonella typhimurium indicated that they exerted an inhibitory effect on frame-shift and base pair type mutations that might contribute to the induction of tumors (Wongwattanasathien *et al.,* 2010). (Haruka *et al*., (2011) reported that EtOAc and n-BuOH fractions of MeOH extract *R. nasutus* roots are enriched with antitumor substances.

Antiproliferative activity

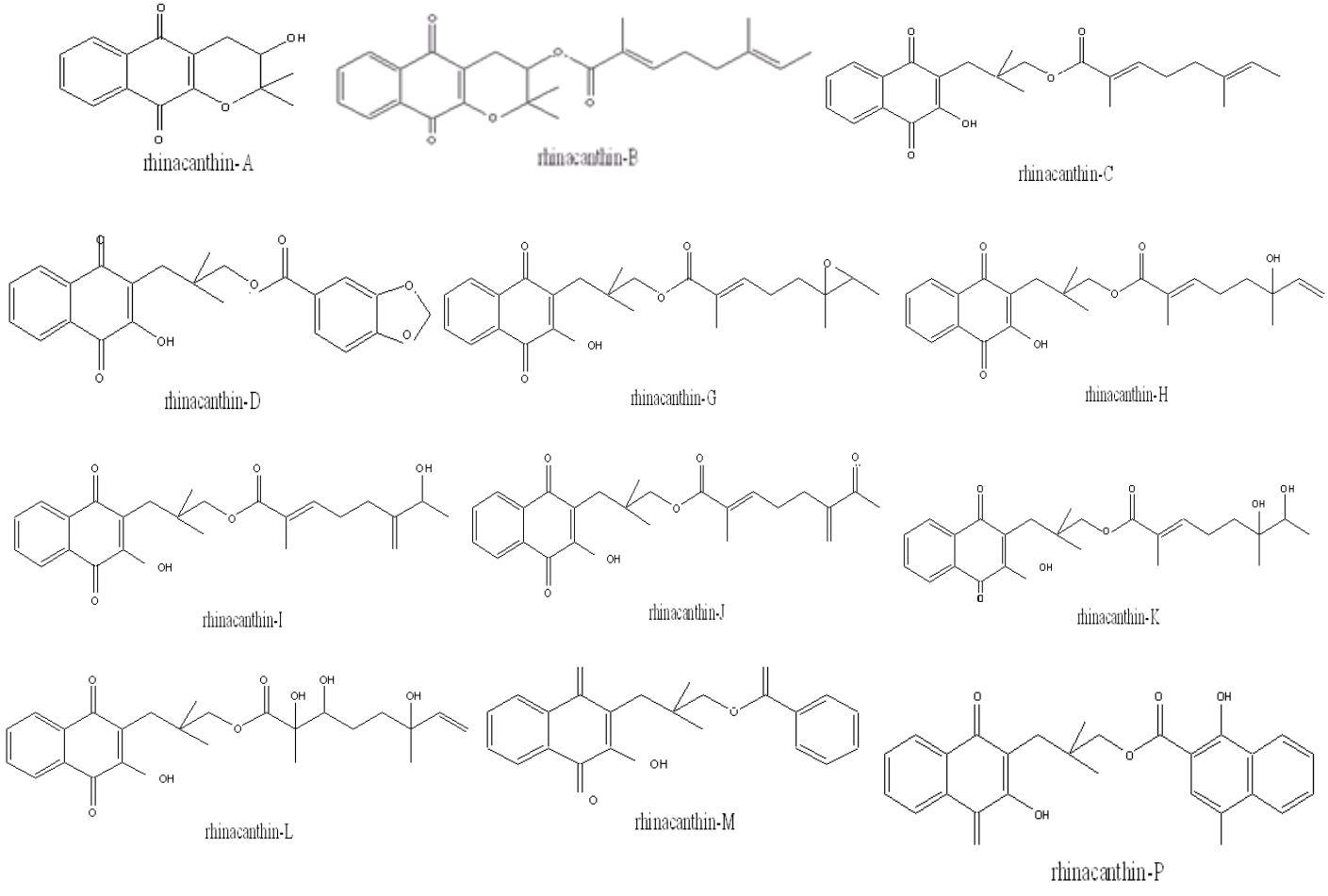
Gotoh and his group had studied *in vitro* antiproliferative activity of leaf and root extract of R. nasutus and rhinacanthin-C against human cervix adenocarcinoma (HeLa), MDR 1 overexpressing subline of human cervical carcinoma (Hvr100-6), human prostatic cancer cell (PC-3), and human bladder carcinoma (T24) cell lines (Gotoh *et al*., 2004).

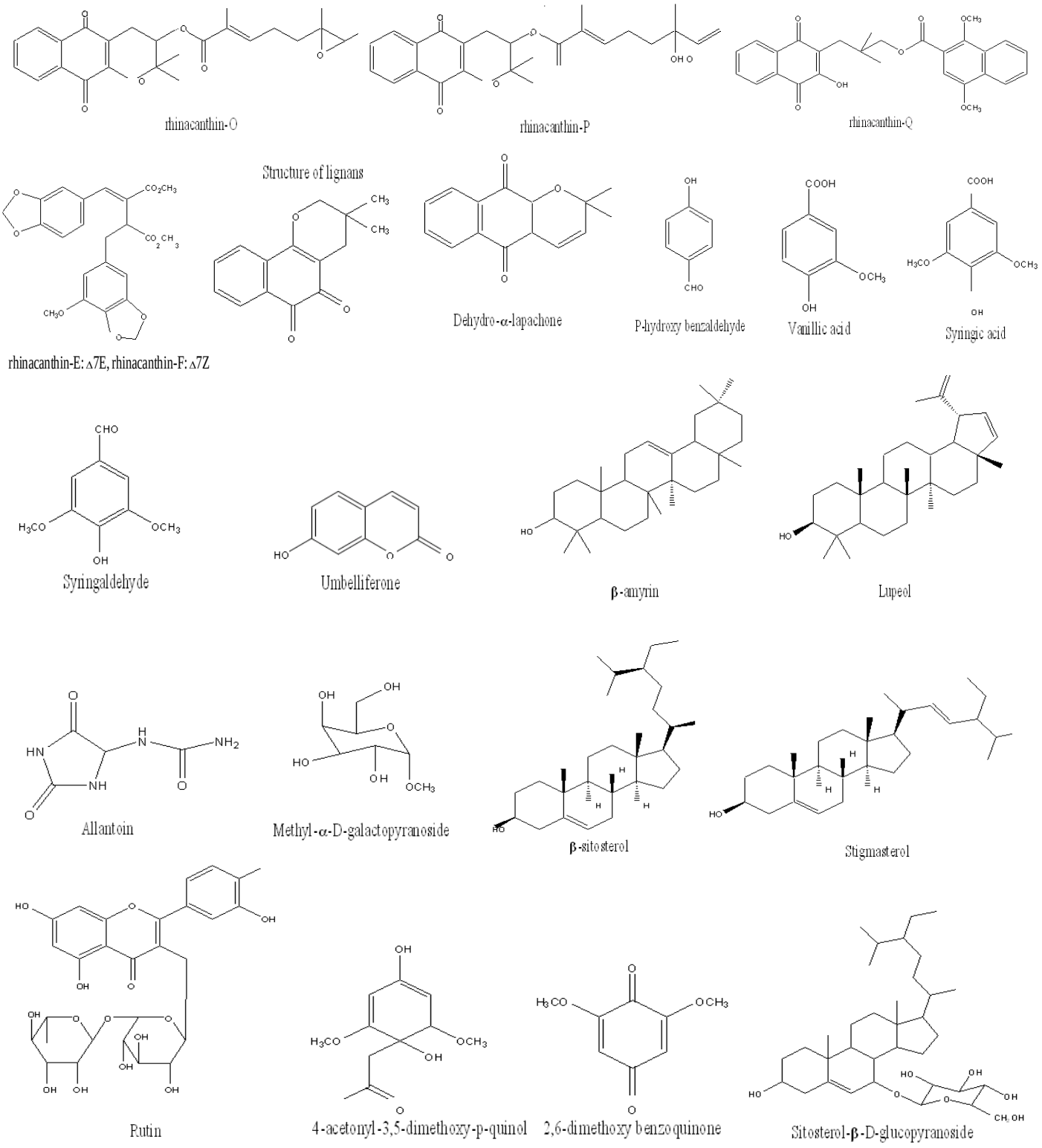
In vivo antiproliferative activity was also observed Sarcoma 180-bearing ICR mice were used to assess the experiment. The ethanol extract of root and aqueous extract of leaves of *R.nasutus* showed significant antiproliferative activity with inhibition of 52.5 % and 44.2 %, respectively (Gotoh *et al*., 2004).

Rhinacanthin-C, -N, and -Q isolated from the roots of *R. nasutus* were capable of inhibiting cell proliferation and induced apoptosis of human cervical carcinoma (HeLS3) cells in a dose and time dependent manners (Siripong *et al*., 2006).

Anti inflammatory activity

The Ethyl acetate extract of *R.nasutus* exhibited the most efficacious anti-inflammatory activity against monocytes from healthy human cells and the methanol extract showed highly specific efficacious anti-inflammatory activity against the multi drug-resistant cells. In the previous studies *R.nasutus* reported that it contains naphthoquinone–rhinacanthin derivatives which





pharmacological potential antiinflammatory activity through inhibition of iNOS and COX-2 gene expressions against LPS-induced release of nitric oxide (NO), PGE2 and TNF-α in RAW 264.7 cells (Nisarat *et al*., 2010).

Immunomodulatory activity

The ethanol extract of *R.nasutus* leaf and stem with lipopolysaccharide (LPS) exhibited an induction of NO and TNF-α production. These may augment macrophage function and thus contribute to cytotoxicity towards viruses, other pathogens and tumor cells (Punturee *et al.,* 2004). The immunological properties of *R. nasutus* have been demonstrated; with *R. nasutus* increasing the proliferation of peripheral blood mononuclear cells, and increased PHA stimulated IL-2 and LPS stimulated TNF-α (Punturee *et al*. 2005).

Hepatoprotective activity

R. nasutus root extract showed hepatoprotective effect in

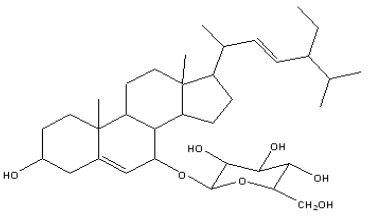
rats treated with aflatoxin B1. Aflatoxin B1 causes its hepatotoxic effects in liver cells by oxidative stress, which causes damage to DNA, proteins and lipids. It has been suggested that *R. nasutus* afforded the hepatocyte protection through an antioxidant mechanism (Shyamal *et al*., 2010).

Antioxidant activity

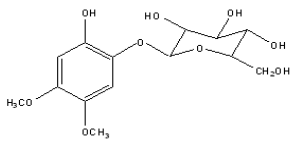
Food, cosmetics, and pharmaceuticals containing *R.nasutus* extract are reported to have antioxidant activity. The mechanism is to remove superoxide from the human body. Cosmetic containing the extract may be useful to reduce aging and hair loss (Wiart *et al.*, 2000). *R. nasutus* has previously been shown to protect skin cells against INF-γ and TNF-α induced apoptosis, potentially through an antioxidant mechanism (Thongrakard *et al*., 2010), furthermore other studies have shown *R. nasutus* to have free radical savaging capabilities (Upendra *et al*., 2010) and nitric oxide (NO) modulating activities when added to mouse macrophages in conjunction with LPS (Punturee *et al*., 2004). James *et al*., (2011) used H2DCFDA staining and showed that *R. nasutus* reduce reactive oxygen species production in HT-22 cells.

Antiplatelet activity

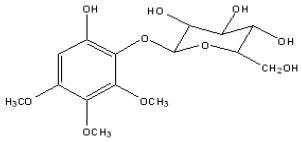
Teng *et al*., (1992) stated that, the *R.nasutus* plant extract possesses the anti-platelet effect. It was confirmed by the anti-platelet aggregation assays. The antiplatelet aggregation of naphthoquinone isolated from the roots of R.nasutus including rhinacanthin-A, -B, -C, -G, -H, -I, -K, -M, and -Q has been reported. These compounds demonstrated inhibition of rabbit platelet aggregation induced by arachidonic acid (100 mM). Rhinacanthin-A, -B, and -C (10 µg/mL) showed inhibition of the rabbit platelet aggregation induced by collagen, while rhinacanthin-B (2 ng/mL) inhibited platelet aggregation induced by platelet activation factor (Wu *et al.*, 1998 b).



Stigmasterol-β-D-glucopyranoside



3,4-dimethylphenol-β-D-glucopyranoside



3,4,5-trimethylphenol-β-D-glucopyranoside

CONCLUSION

R.nasutus has been ethnomedicinally used as a therapeutic agent for a variety of diseases, as we have illustrated in this article. Moreover, numerous research works have proven its uses beyond the ethnomedicines. Flavonoids, steroids, terpenoids, anthraquinones, lignans and especially naphthoquinone analogues which were isolated from this plant may be responsible for its pharmacological activities. The road ahead is to establish specific bioactive molecules and its mode of action, which might be responsible therapeutic efficacy. Therefore further pharmacological exploration of *R.nasutus* is essential.

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