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REVIEW ARTICLE

The Genus *Glycosmis* [Rutaceae]: A Comprehensive Review on its Phytochemical and Pharmacological Perspectives

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ARTICLE HISTORY

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Abstract: ***Background*:** Medicinal plants are rich source of large variety of lead compounds. The plants of genus *Glycosmis* or its different parts valued for its therapeutic and medicinal qualities. *Glycosmis* belongs to the family Rutaceae.

***Objective*:** The genus *Glycosmis* is a rich source of pharmacologically and biologically active secondary metabolites, such as alkaloids, flavonoids, phenolic glycosides, quinones, terpenoids, glycerides isolated from different parts of *Glycosmis* plant. The objectives of this review is to provide updatedand complete information on the distribution, phytochemical, pharmacological, and toxicity research of *Glycosmis s*pecies.

***Results*:** About 233 phytoconstituents are isolated from this genus. Recent interest in this genus has focused on isolating and identifying of different phytoconstituents that exhibit potent antioxidant, antibacterial, antiviral and anticancer activities. They show good cytotoxic activity against various cancer cell lines and also reported for good antiviral and immunomodulatory activity. In this support convincing evidence in experimental animal models are available.

***Conclusion*:** This review summarizes information about the isolated compounds their bioactivities related to same compounds present in other plants including pharmacological activities of plant extract of *Glycosmis* genus.

Keywords: *Glycosmis* genus, cytotoxicity, phytochemistry, pharmacology, medicinal plants, biologically active secondary metabolites.

1. INTRODUCTION

Ayurveda, Unani, and Siddha utilize plant products or extracts for disease treatment, more than 20,000 species of medicinal plant listed by World Health Organization [WHO] are used globally [1]. There is a continuous need to search for new sources of pharmaceutically active substances and rising interest in medicinal plants. Worldwide research on plant species used in local or foreign traditional medicine is increasing. The plants of genus *Glycosmis* or its different parts are valued for its therapeutic and medicinal qualities. *Glycosmis* belongs to the Rutaceae family, commonly known as citrus family [2] usually placed in the order Sapindales. The plant list includes 108 scientific plant names of species rank for the genus *Glycosmis,* out of which 50 are accepted species names [2]. Plants of this genus are shrubs and small trees characterized by flowers that divide into four or five parts, usually with strong essences.

The aim of this paper is to accumulate information about the phytoconstituents along with their pharmacological activities and also to compile various pharmacological studies of the different plants of the *Glycosmis*.

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2. BOTANICAL DESCRIPTION

2.1. Diversity

There are about 35 to 50 species included in the genus, but here in this review we have described about 21 species viz: *Glycosmis arborea, Glycosmis bilocularis, Glycosmis chlorosperma, Glycosmis citrifolia, Glycosmis cochinchinensis, Glycosmis craibii, Glycosmis crassifolia, Glycosmis cyanocarpa, Glycosmis elongate, Glycosmis macrophylla, Glycosmis mauritiana, Glycosmis montana, Glycosmis parva, Glycosmis parviflora, Glycosmis pentaphylla, Glycosmis petelotii, Glycosmis pseudoracemosa, Glycosmis puberula, Glycosmis sapindoides, Glycosmis stenocarpa and Glycosmis trichanthera.*

2.2. Taxonomy

Kingdom:	Plantae
Order:	Sapindales
Family:	Rutaceae
Subfamily:	Aurantioideae
Tribe:	Clauseneae
Genus:	Glycosmis

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2.3. Common Names

English: Orangeberry, Gin Berry, Toothbrush Plant

French: Glycosmisier De Cochinchine.

Chinese: Shi Ling Ju, Shan Xiaoju

Tagalog/Filipino: Gingging

Thai: Khoeitai, Lukkhoei Tai.

Malaysia: Napan, Nerapan, Merapi.

Sanskrit: Asvasakhotah, Kupiluh.

Hindi: Ban Nimbu.

Kannada: Gunaamani, Guroda,

Malayalam: Kuttippanal, Panal.

Tamil: Anam.

2.4. Botanical Characteristics of *Glycosmis* Species

Unarmed small trees or shrubs; new growth covered with dense, usually ferruginous pubescence; leaves 1-foliolate, 3-foliolate, or odd-pinnate; leaflets with short petiolules, alternate, long-lanceolate, more or less coriaceous; inflorescences compound, often densely racemose; flowers small, 5-merous; sepals united to the middle, with broad imbricate lobes; petals 5, white, long-elliptical or oval, imbricate; stamens 10, filaments subulate, broadened below, anthers small, often with oil glands on the back and tip; disk annular or cylindric; ovary 2-5-locular, with 1 ovule in each locule; style very short and thick, persistent, stigma simple or disk shaped; fruit a juicy berry or dry; seeds oval, thick, with a membrane ceoustesta; embryo with fleshy plano-convex cotyledons and a very short plumule [3].

Simple Leaf, or unifoliate, rarely or some 2-3-foliolate leaves mingled with predominately unifoliate ones [*Glycosmis crassifolia, Glycosmis parva, Glycosmis pseudoracemosa*], few leaflets, usually 3, rarely 2, 4, or 5 [*Glycosmis elongate, Glycosmis mauritiana, Glycosmis trichanthera*], blunt leaflets apex, broadly obtuse, rounded, or retuse [*Glycosmis parva*], inflorescence elongated, rather many flowered, usually longer than the petiole or petiole to the first leaflet [*Glycosmis elongate, Glycosmis parviflora, Glycosmis pentaphylla, Glycosmis pseudoracemosa*], short stocky ovary with 5 locules leaves of 2 or 3 leaflets, and glabrous petals [*Glycosmis puberula*], flowers constantly 4-merous [with 8 stamens and 4-locular ovary][*Glycosmis cyanocarpa, Glycosmis trichanthera*]. Ovary predominantly 2-3-locular, sometimes 4-locular, but never 5-locular [*Glycosmis elongata, Glycosmis parva, Glycosmis pseudosapindoides*], fruits longer than wide, oblong, ellipsoid, ovoid, or obvoid [*Glycosmis cyanocarpa, Glycosmis pseudosapindoides, Glycosmis sapindoides*], fruits as long as wide or depressed, more or less globose [*Glycosmis pseudosapindoides, Glycosmis elongata*]

2.5. Distribution [2, 4]

Glycosmis bilocularis: India, Ceylon:

Glycosmis chlorosperma: Thailand, Laos, Viet Nam, S China, Hainan, S Burma, Java.

Glycosmis cochinchinensis: Burma, Cambodia, China, Laos, Thailand, Vietnam

Glycosmis crassifolia: Malaysia.

Glycosmis cyanocarpa: India, Nepal, S Tibet, Bangladesh, Burma, Srilanka, Thailand, Malaysia, Philippines, Indonesia [western].

Glycosmis elongate: Java

Glycosmis macrophylla: India.

Glycosmis mauritiana: India, Burma, Thailand, Malaya, Hainan, Mauritius.

Glycosmis montana: India, China, Java, Hainan, Borneo, Philippines.

Glycosmis parva: Thailand

Glycosmis parviflora and *Glycosmis citrifolia*: China, Florida, Jamaica, Cuba, Tropical America, Java.

Glycosmis pentaphylla and *Glycosmis arborea*: India, Burma, Thailand, Malaya, Ceylon, Nepal, Malaysia.

Glycosmis petelotii: Vietnam.

Glycosmis pseudoracemosa: South China, Vietnam.

Glycosmis puberula and *Glycosmis craibii*: Thailand, Malay Peninsula, Vietnam.

Glycosmis sapindoides: India, Malay Peninsula, Thailand, West Iran, Australia, Borneo.

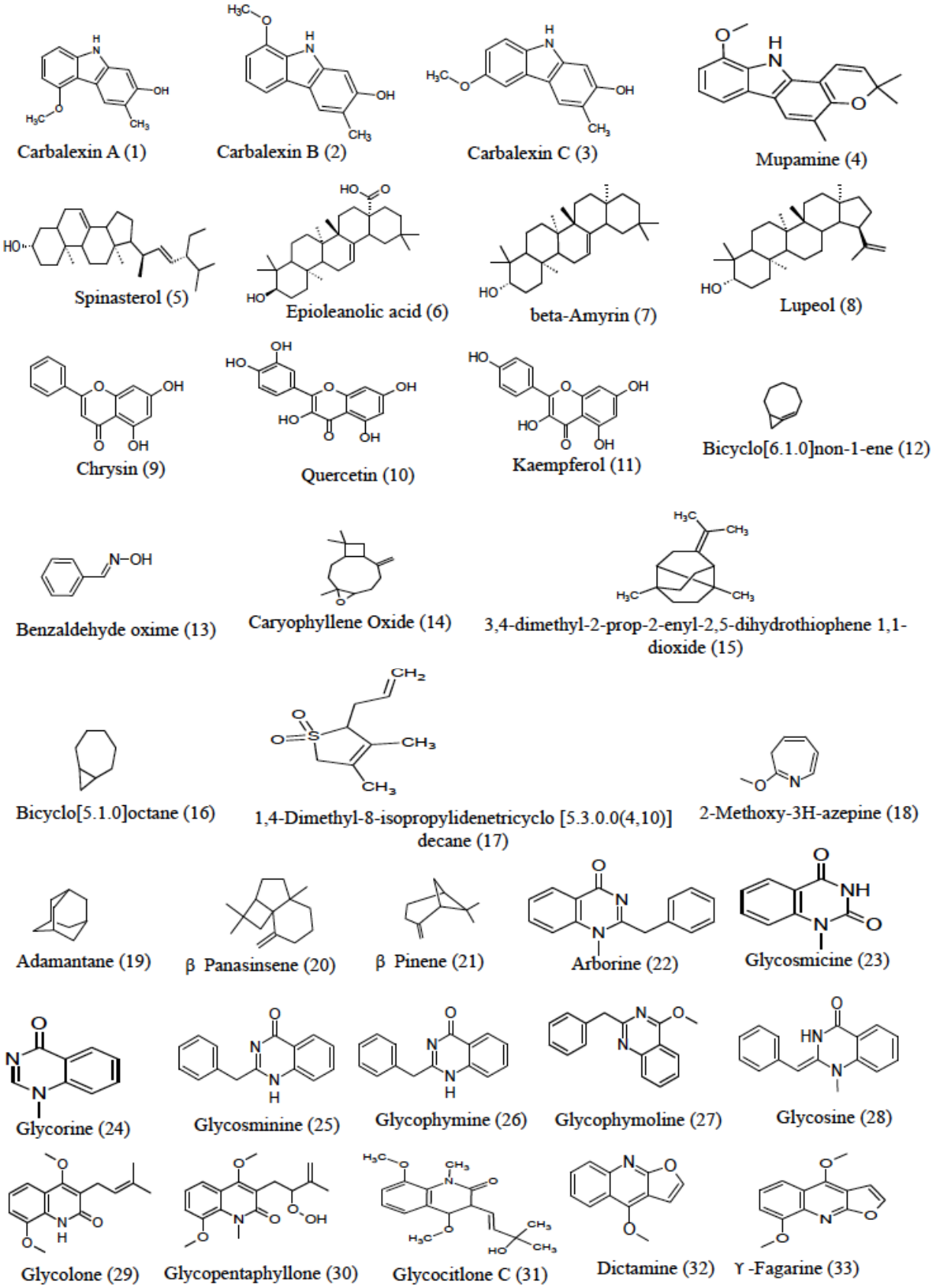
Glycosmis stenocarpa: Vietnam.

Glycosmis trichanthera: Vietnam, Burma, Malay Peninsula, Sumatra, Thailand, Malaysia.

3. PHYTOCHEMISTRY

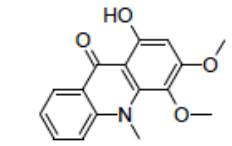
The detailed distributions of chemical constituents present in different parts of *Glycosmis* species are given in Table **1** and Fig. (**1**).

The compounds isolated from the extracts of *Glycosmis spp.* have been studied for their biological activities. Dictamine (**32**) (*Glycosmis pentaphylla, Esenbeckia leiocarpa*) exhibits acetylcholinesterase inhibition activity [4]. Tachioside (**47**) (*Glycosmis pentaphylla*) has been reported to inhibit nitric oxide production in lipopolysaccharides-stimulated RAW 264.7 cells [5]. N-methylated derivatives of Glycosmicine (**23**) (*Glycosmis pentaphylla*) compounds exhibit anticonvulsant, antioxidant activity [6] and antinociceptive activity [7]. Glycosine (**28**), Glycorine (**24**) and Glycosminine (**25**) (*Glycosmis pentaphylla*) have been studied to possess antimicrobial, anticancer and antinociceptive activities [7]. Glycophymoline (**27**) (*Glycosmis pentaphylla*) possesses antinociceptive activity [8]. Glycopentaphyllone (**30**) (*Glycosmis pentaphylla*) has been observed to show antibacterial activity [9]. Glypentoside B (**36**) and Glypentoside C (**37**) (*Glycosmis pentaphylla*) show antimicrobial activity [10]. Evolitrine (**231**) (*Glycosmis cyanocarpa*) has the property of inhibition of carrageenan induced rat paw edema in rats [11]. Thalebanin B (**227**) (*Glycosmis crassifolia*) and dehydrothalebanin A (**228**) (*Glycosmis crassifolia*) have significant antifungal activities [11, 12]. Dehydroniranin A (**230**) and dehydroniranin B (**229**) (*Glycosmis cyanocarpa*),

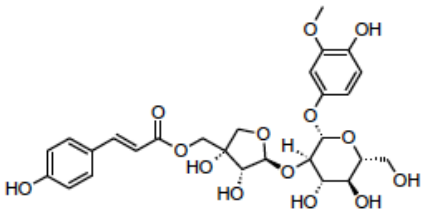


Phytoconstituents of *Glycosmis pentapylla*

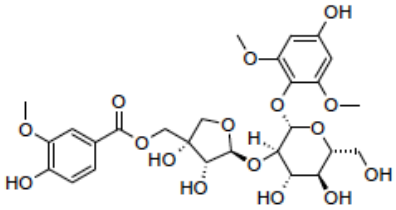
Fig. (1) contd….



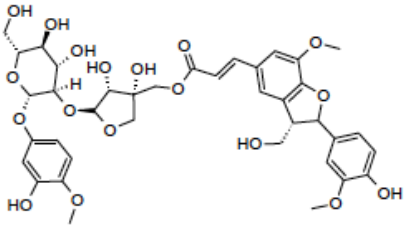
1-Hydroxy-3,4-dimethoxy
-10-methylacridan-9-one (34)



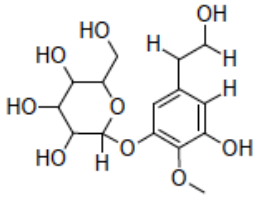
Glypentoside A (35)



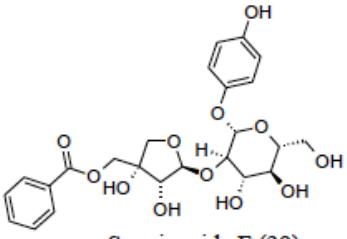
Glypentoside B (36)



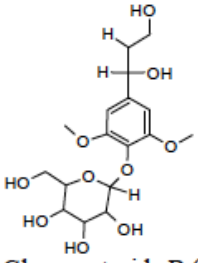
Glypentoside C (37)



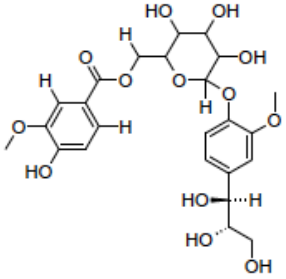
Glycopentoside A (38)



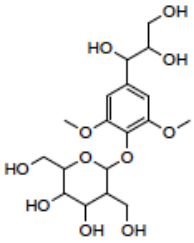
Seguinoside F (39)



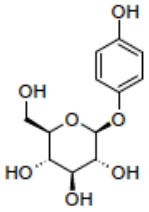
Glycopentoside B (40)



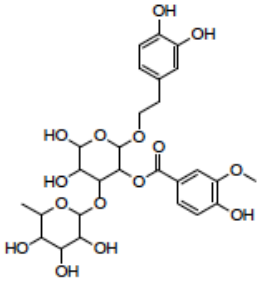
Glycopentoside C (41)



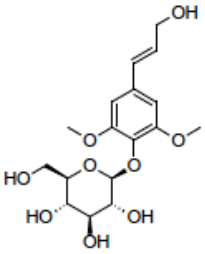
threo-1-C-syringylglycerol
4-O-b-D-glucopyranoside (42)



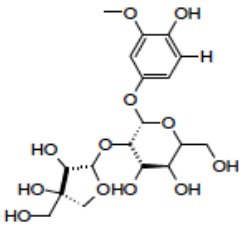
Arbutin
(43)



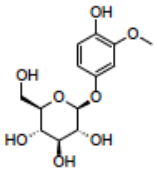
Sequinoside K (44)



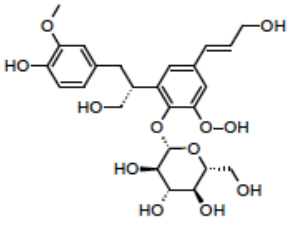
Syringin (45)



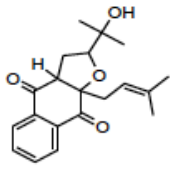
Markhamioside F (46)



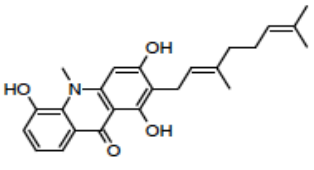
Tachioside (47)



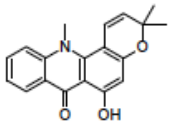
Icariside E5 (48)



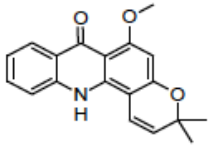
Glycoquinone (49)



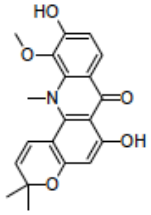
Glycocitrine-III (50)



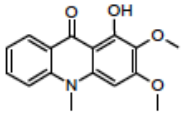
Noracronycine (51)



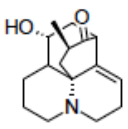
des-N-methylacronycine (52)



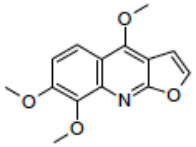
Citracridone-I (53)



Arborinine (54)



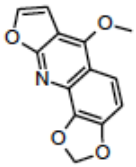
Acrifoline (55)



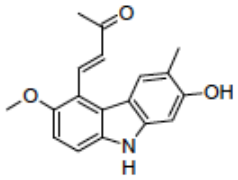
Skimmianine (56)

Phytoconstituents of *Glycosmis pentapylla*

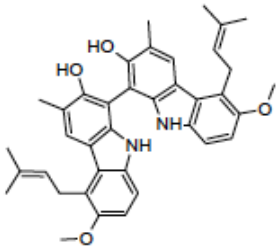
Fig. (1) contd….



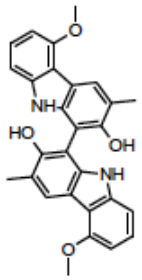
Kokusagine (57)



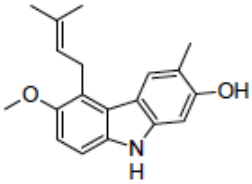
4-(7-Hydroxy-3-methoxy-6-methyl-9H-carbazol-4-yl) but-3-en-2-one (58)



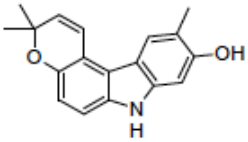
Bisglybomine B (59)



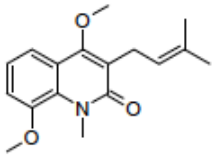
Biscarbalexine A (60)



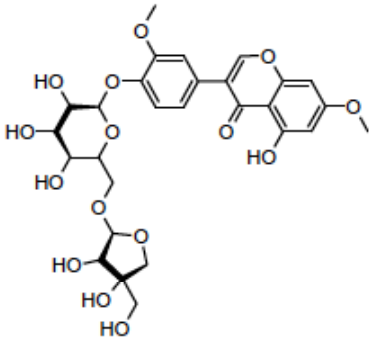
Glybomine B (61)



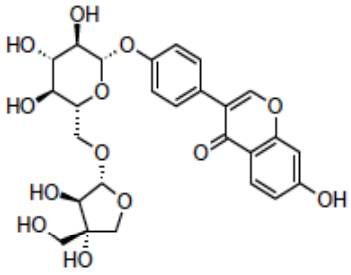
Glycoborinine (62)



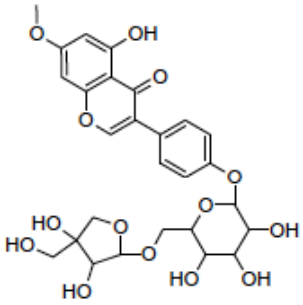
4,8-Dimethoxy-1-methyl-3-(3-methylbut-2-en-1-yl) quinolin-2(1H)-one (63)



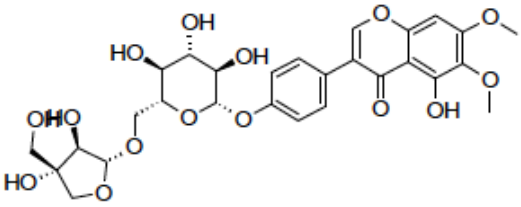
4′,5-Dihydroxy-3′,7-dimethoxyisoflavone 4′-*O*-α-D-apiofuranosyl-(1->6)-α-D-glucopyranoside (64)



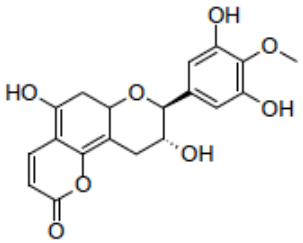
7-Hydroxy-4'-methoxyisoflavone 7-O-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside (65)



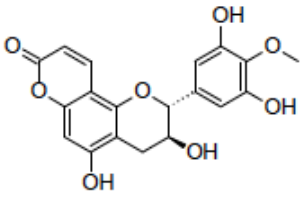
Coromandelin (66)



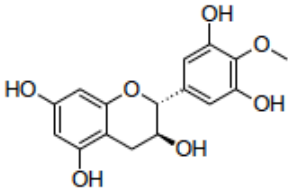
4',5-Dihydroxy-6,7-dimethoxyisoflavone 4′-*O*-α-D- apiofuranosyl-(1->6)-α- D-glucopyranoside (67)



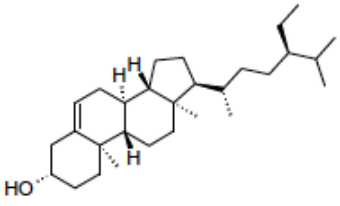
Glycoflavanones A (68)



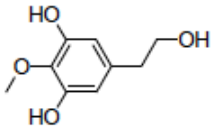
Glycoflavanones B (69)



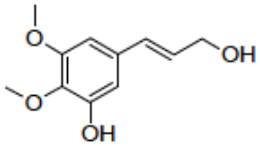
4′-O-methylgallocatechine (70)



β-sitosterol (71)



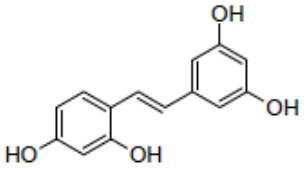
Alphitol (72)



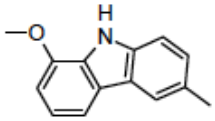
3,4-Dimethoxy-5-hydroxy-trans-cinnamyl alcohol (73)

Phytoconstituents of *Glycosmis pentapylla*

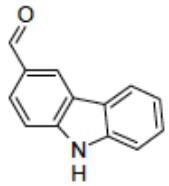
Fig. (1) contd….



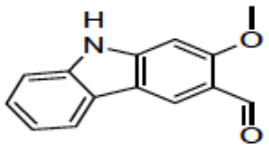
Oxyresveratrol (74)



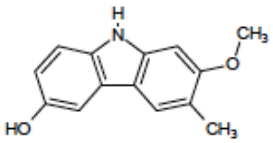
Glycozolicine (75)



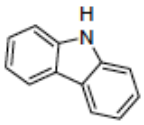
3-Formylcarbazole (76)



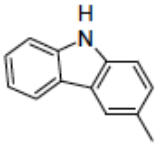
Glycosinine (77)



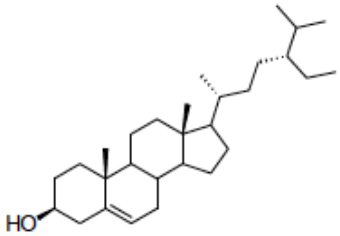
Glycozolidol (78)



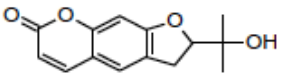
Carbazole (79)



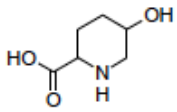
3-methylcarbazole (80)



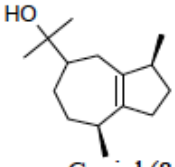
gamma-Sitosterol (81)



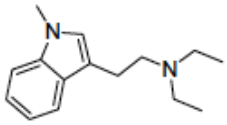
Marmesin (82)



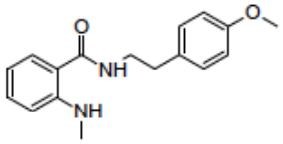
5-Hydroxypipecolic acid (83)



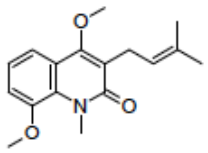
Guaiol (84)



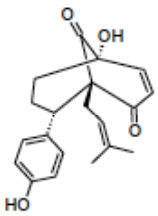
1H-Indole-3-ethanamine (85)



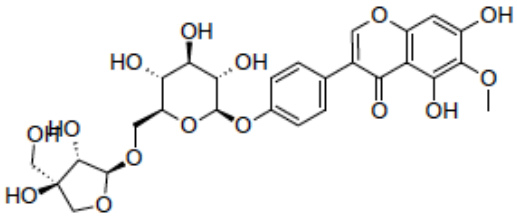
des-N-methylnoracronycine (131)



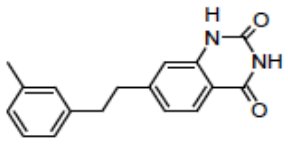
3-(3′,3′-Dimethylallyl)-
4,8-dimethoxy-N-methyl-
Quinolin-2-one (184)



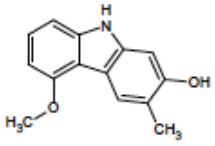
Acutifolin A (197)



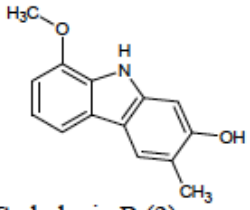
Tectorigenin 4′-*O*-α-D- apiofuranosyl-
(1->6)-α- D-glucopyranoside (232)



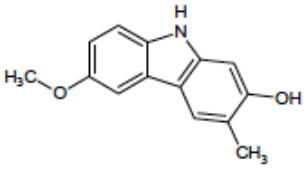
1-Methyl-3-(2-phenylethyl)
quinazoline-2,4(1H,3H)-diones
(233)



Carbalexin A (1)



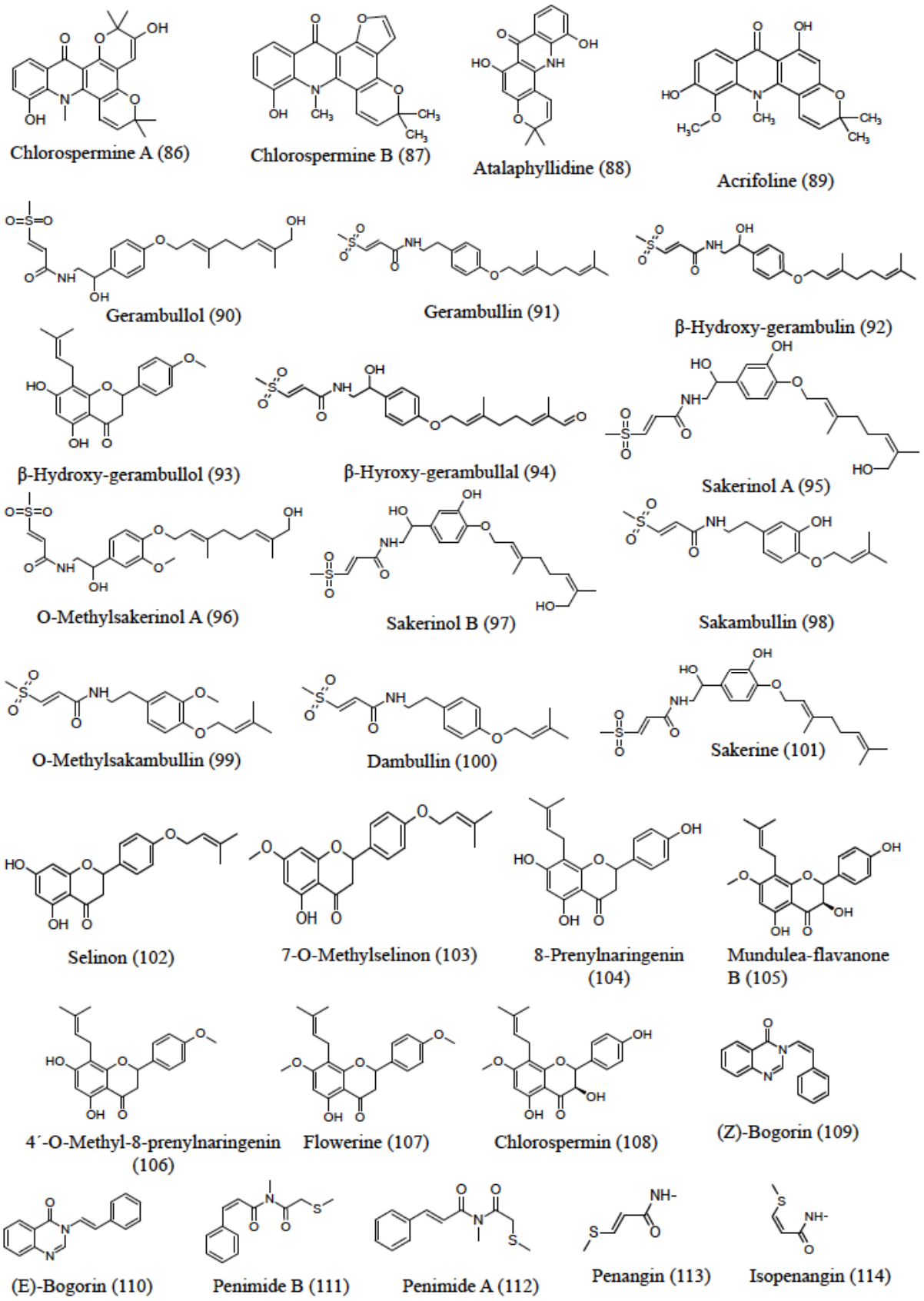
Carbalexin B (2)



Carbalexin C (3)

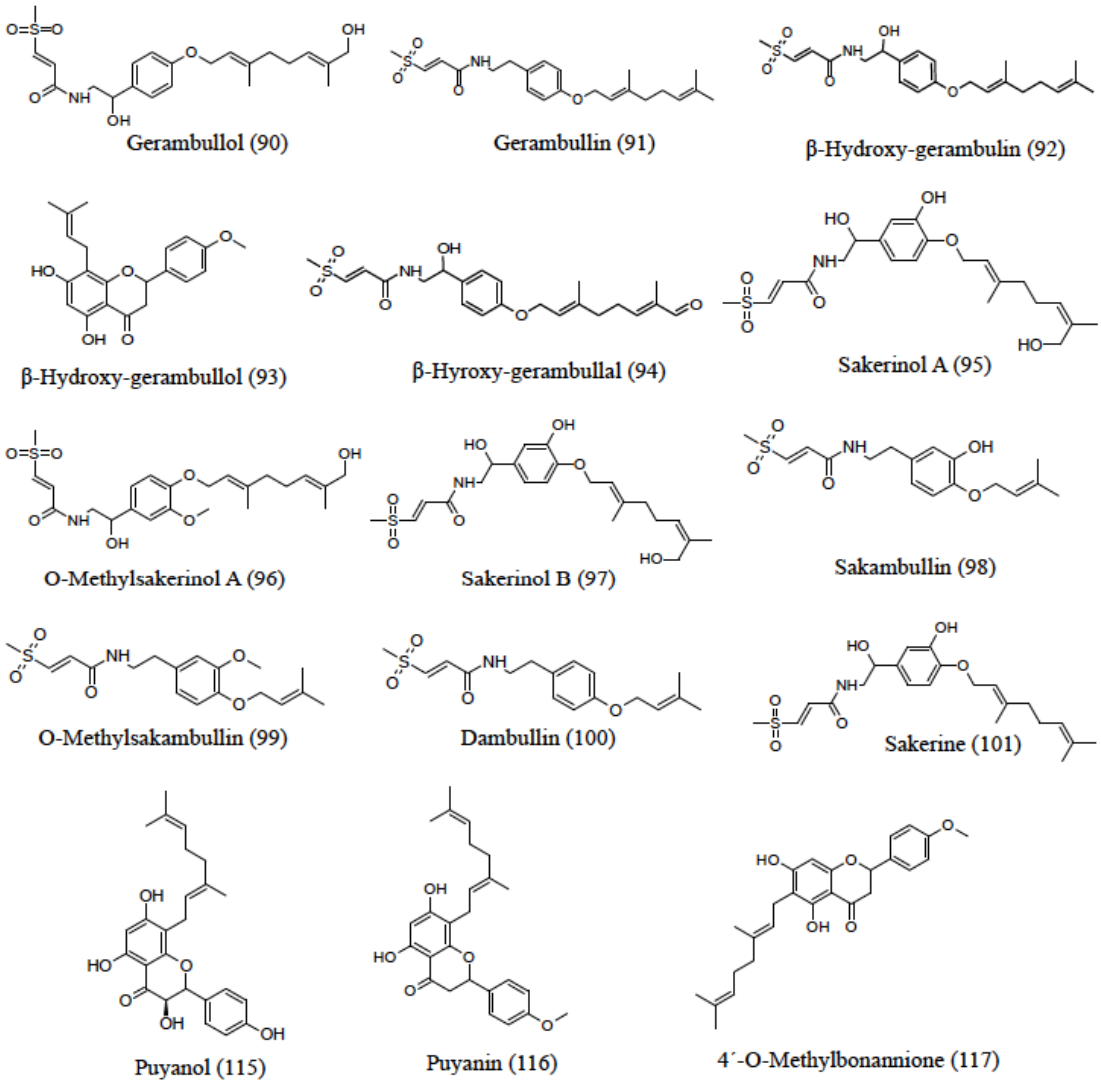
Phytoconstituents of *Glycosmis parviflora*

Fig. (1) contd….



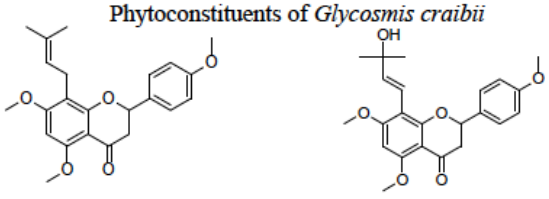
Phytoconstituents of *Glycosmis chlorosperma*

Fig. (1) contd….



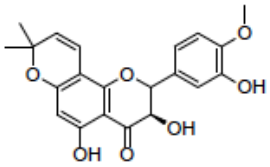
Phytoconstituents of *Glycosmis pseudoracemosa*

Phytoconstituents of *Glycosmis craibii*



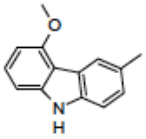
Phytoconstituents of *Glycosmis puberula*

Fig. (1) contd….

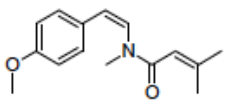


Glysapinol (122)

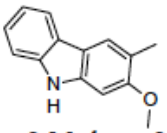
Phytoconstituents of *Glycosmis sapindoides*



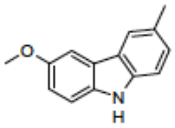
Glycrophylamine (123)



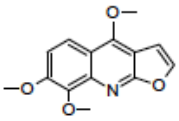
Glycrophylamide (124)



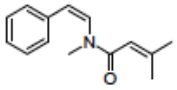
2-Methoxy-3-Methylcarbazole (125)



Glycozoline (126)

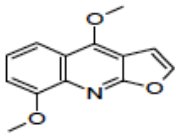


Skimianine (127)

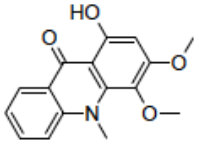


Dehydrothalebanin B (128)

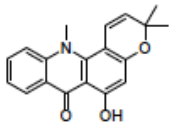
Phytoconstituents of *Glycosmis macrophylla*



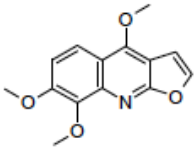
gamma-Fagarine (33)



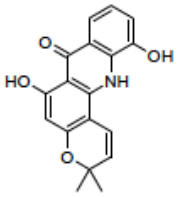
1-Hydroxy-3,4-dimethoxy -10-methylacridan-9-one (34)



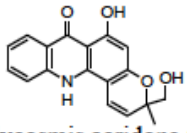
Noracronycine (51)



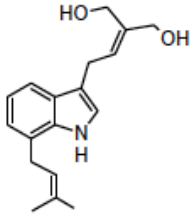
Skimmianine (56)



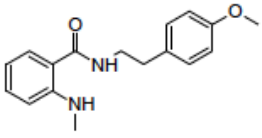
Atalaphyllidine (88)



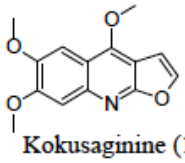
Glycosmis acridone (129)



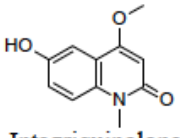
Glycosmisindole (130)



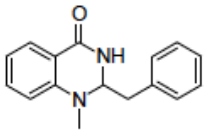
des-N-methylnoracronycine (131)



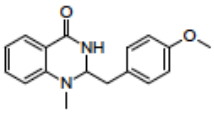
Kokusaginine (132)



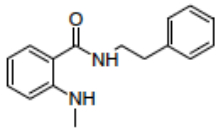
Integriquinolone (133)



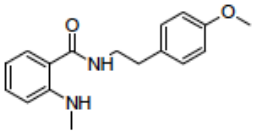
Glycozolone-A (134)



Glycozolone-B (135)



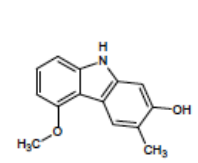
Glycoamide-A (136)



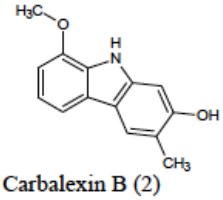
Glycoamide-B (137)

Phytoconstituents of *Glycosmis cochinchinensis*

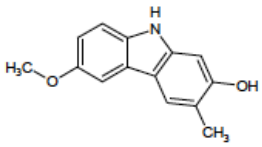
Fig. (1) contd….



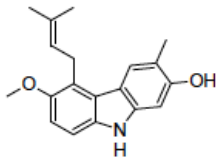
Carbalexin A (1)



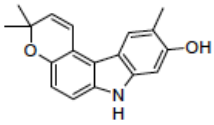
Carbalexin B (2)



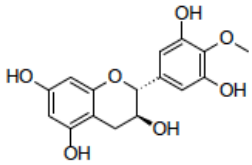
Carbalexin C (3)



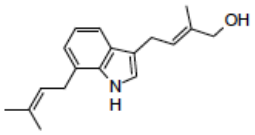
Glybomine B (61)



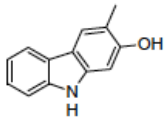
Glycoborinine (62)



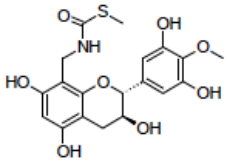
4′-O-methylgallocatechine (70)



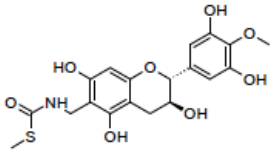
(E)-3-(3-hydroxymethyl-2-butenyl) -7-(3-methyl-2-butenyl)-1H-indole (138)



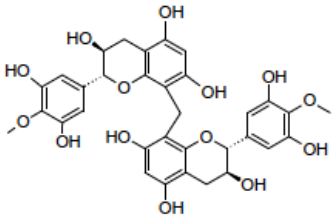
2-Hydroxy-3-methyl -9 H-carbazole (139)



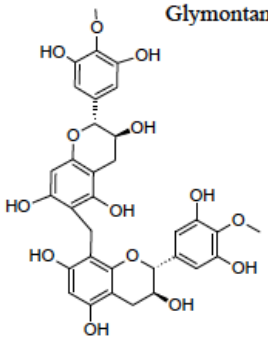
Glymontanine A (140)



Glymontanine B (141)

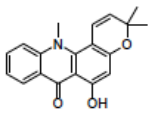


Montahomobisflavan A (142)

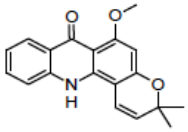


Montahomobisflavan B (143)

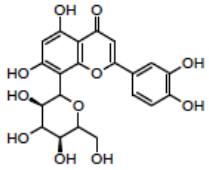
Phytoconstituents of *Glycosmis Montana*



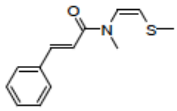
Noracronycine (51)



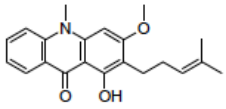
des-N-methylacronycine (52)



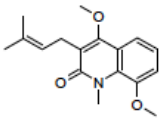
Luteolin 8-C-beta- D-glucopyranoside (144)



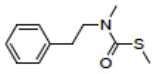
Methylillukumbin B (148)



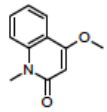
1-Hydroxy-3-methoxy-2- (3-methylbut-2-enyl)-*N*- methylacridan-9-one (145)



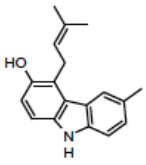
4,8-Dimethoxy-3- (3-methylbut-2-enyl)- *N*-methyl-2-quinolone (146)



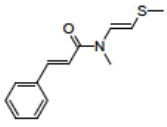
Niranin (147)



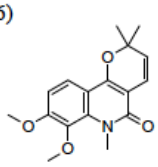
4-Methoxy 1-methyl quinolin-2-one (152)



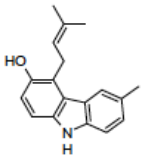
Illukumbin B (149)



Methylillukumbin A (150)



7, 8-Dimethoxy-2,2,6- trimethyl-pyrano quinolin-5-one (151)



Glycomaurrol (156)

Fig. (1) contd….

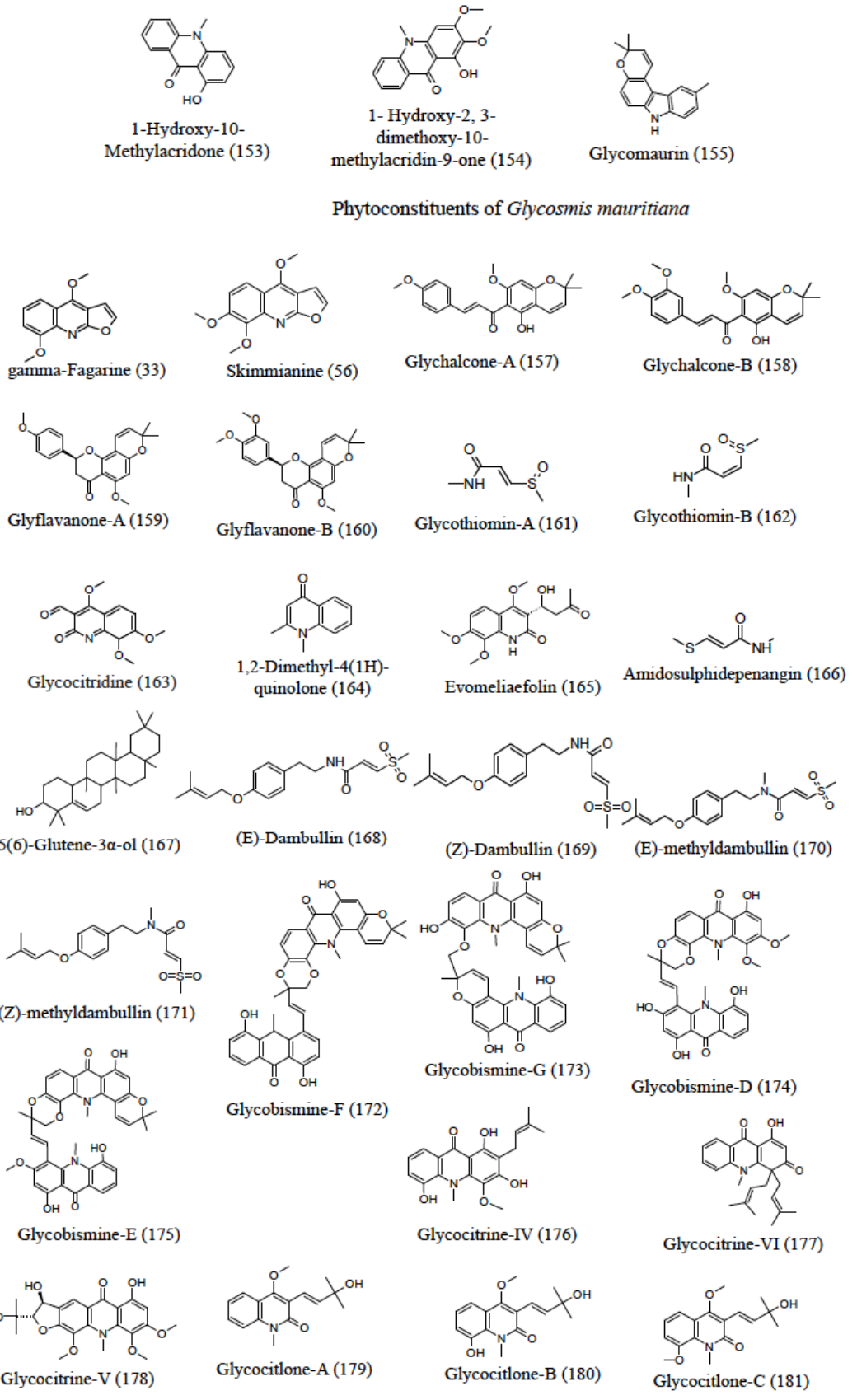
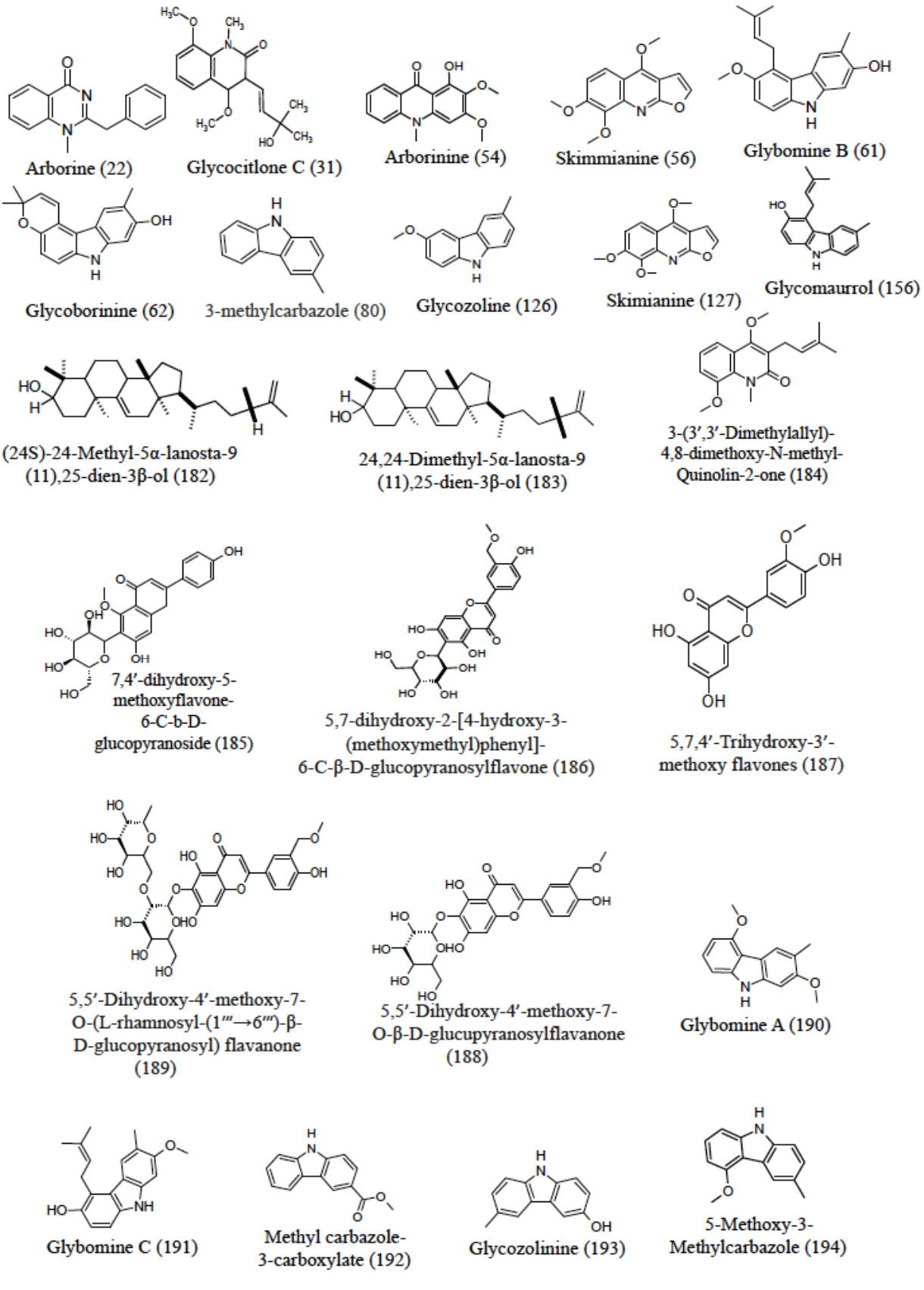
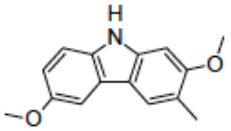

1-Hydroxy-10-Methylacridone (153)
1- Hydroxy-2, 3-dimethoxy-10-methylacridin-9-one (154)
Glycomaurin (155)
Phytoconstituents of *Glycosmis mauritiana*
gamma-Fagarine (33)
Skimmianine (56)
Glychalcone-A (157)
Glychalcone-B (158)
Glyflavanone-A (159)
Glyflavanone-B (160)
Glycothiomin-A (161)
Glycothiomin-B (162)
Glycocitridine (163)
1,2-Dimethyl-4(1H)-quinolone (164)
Evomeliaefolin (165)
Amidosulphidepenangin (166)
5(6)-Glutene-3α-ol (167)
(E)-Dambullin (168)
(Z)-Dambullin (169)
(E)-methyldambullin (170)
(Z)-methyldambullin (171)
Glycobismine-F (172)
Glycobismine-G (173)
Glycobismine-D (174)
Glycobismine-E (175)
Glycocitrine-IV (176)
Glycocitrine-VI (177)
Glycocitrine-V (178)
Glycocitlone-A (179)
Glycocitlone-B (180)
Glycocitlone-C (181)
Phytoconstituents of *Glycosmis citrifolia*

Fig. (1) contd….

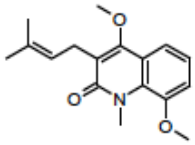


Phytoconstituents of *Glycosmis arborea*

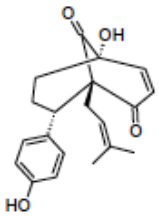
Fig. (1) contd….



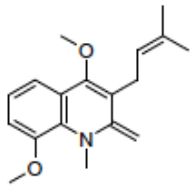
Glycozolidine (195)



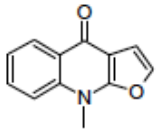
4,8-dimethoxyfuro [2,3-*b*]quinolone (196)



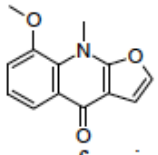
Acutifolin A (197)



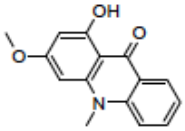
4,8-Dimethoxy-3-(3-methylbut-2-enyl)-*N*-methyl-2-quinolone (198)



Isodictamnine (199)

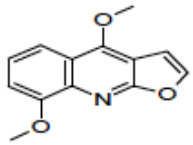


Iso-gamma-fagarine (200)

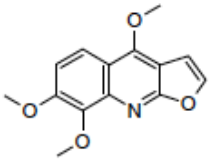


1-Hydroxy-3-methoxy-10-methylacridan-9-one (201)

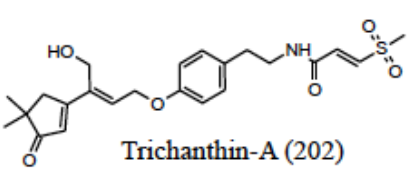
Phytoconstituents of *Glycosmis arborea*



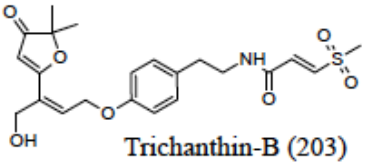
ϒ -Fagarine (33)



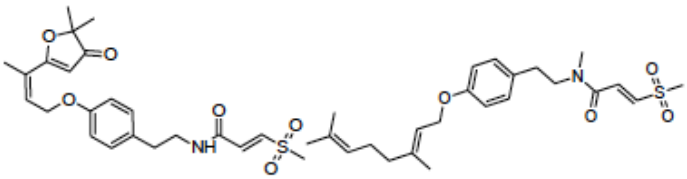
Skimmianine (56)



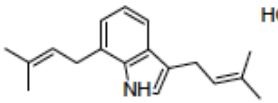
Trichanthin-A (202)



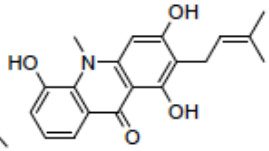
Trichanthin-B (203)



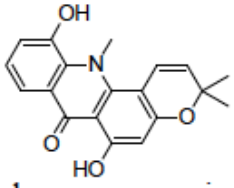
Glyparvin-A (204) Methylgerambullin (205)



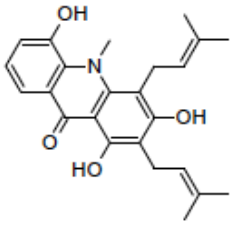
Yukocitrin (206)



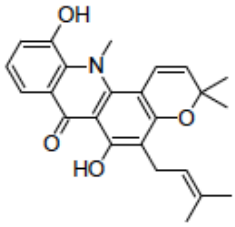
Junosin (207)



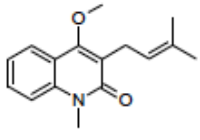
5-Hydroxy-noracronycine (208)



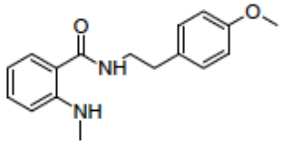
N-methyl-atalaphylline (209)



N-methyl-atalaphyllinine (210)



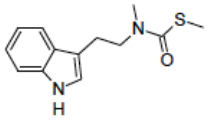
N-methylatanine (211)



des-N-methylnoracronycine (131)

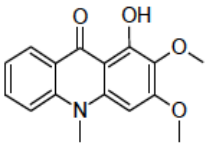
Phytoconstituents of *Glycosmis trichanthera*

Fig. (1) contd….

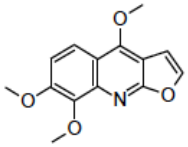


Glypetelotine (212)

Phytoconstituents of *Glycosmis petelotii*

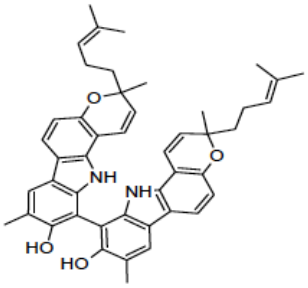


Arborinine (54)



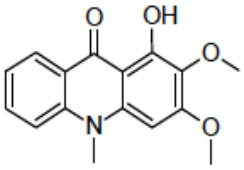
Skimmianine (56)

Phytoconstituents of *Glycosmis elongate*

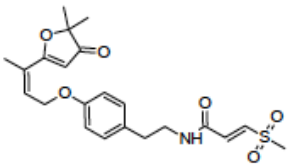


bis-Isomahanine (213)

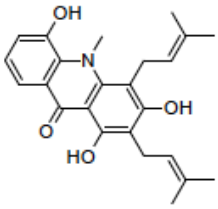
Phytoconstituents of *Glycosmis stenocarpa*



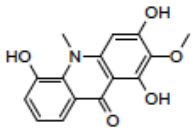
Arborinine (54)



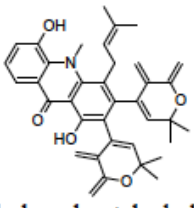
Glyparvin-A (204)



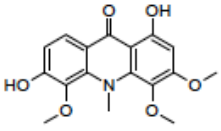
N-methyl-atalaphylline (209)



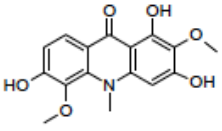
Glycosparvarine (214)



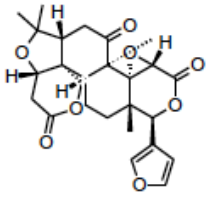
N-methyl-cyclo-atalaphylline-A (215)



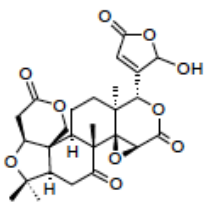
Glycofolinine (216)



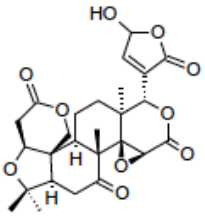
Citramine (217)



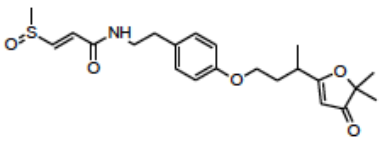
Limonin (218)



Limonexic acid (219)



Iso-limonexic acid (220)



S-deoxy-dihydro-glyparvin (221)

Fig. (1) contd….

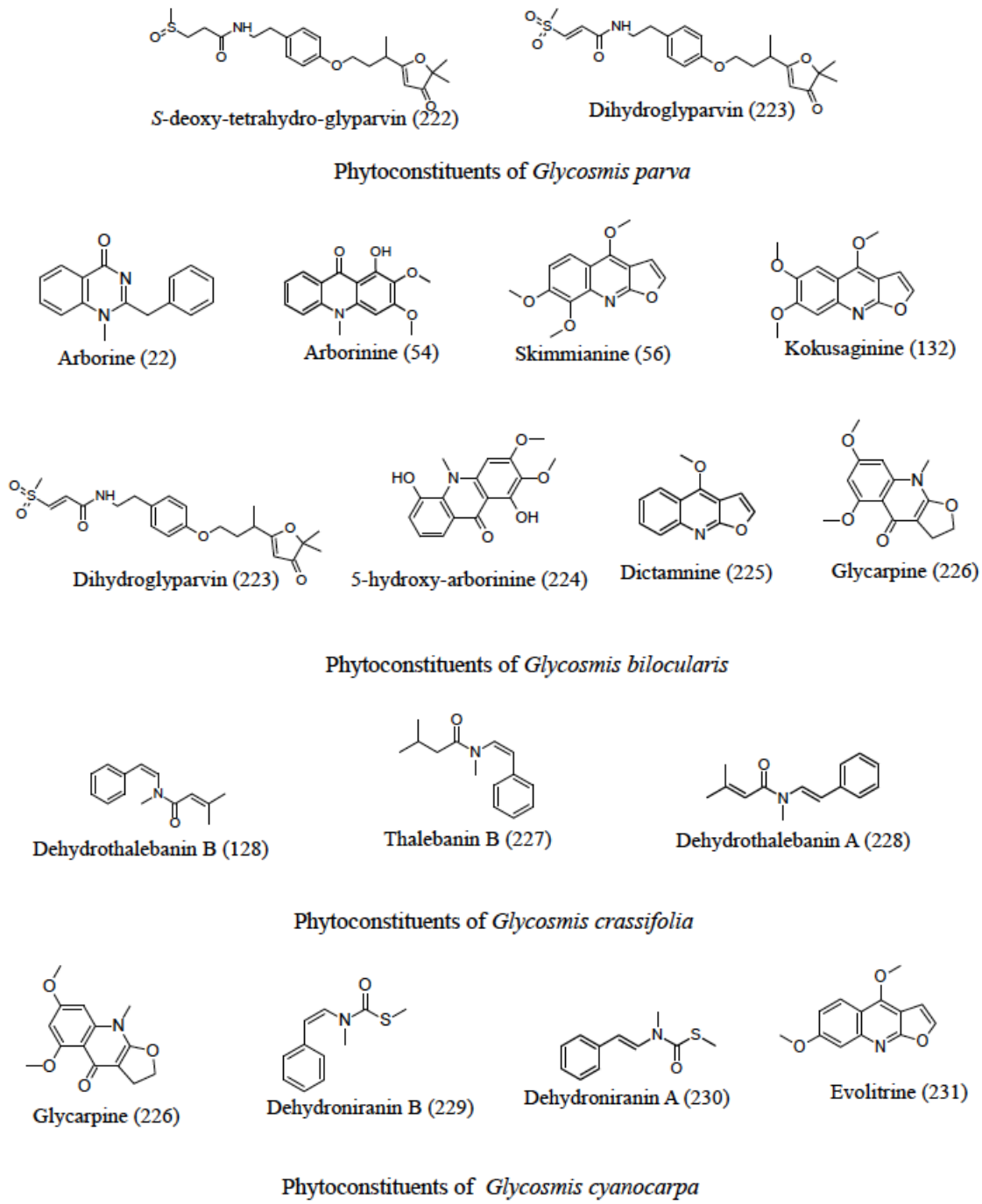


Fig. (1). Chemical Structure of Phytoconstituents present in different species of *Glycosmis*

penangin (**113**) (*Glycosmis chlorosperma*) exhibit antifungal and anti-insecticidal activities [13]. Skimianine (**127**) and arborinine (**54**) (*Glycosmis pentaphylla*, *Glycosmis arborea*, *Glycosmis elongate, Glycosmis parv, and Glycosmis bilocularis*) have been studied to have antiprotozoal activity and cytotoxicity towards L-6 cells [14]. Glycosparvarine (**214**), Glycofolinine (**216**) and dihydroglyparvin (**223**) (*Glycosmis parva*) have been analyzed for their anti-HSV activity in the studies [15]. Arborinine (**54**) (*Glycosmis pentaphylla*, *Glycosmis arborea*, *Glycosmis elongate, Glycosmis parva, Glycosmis bilocularis*) is reported for antiplasmodial and antioxidant activities [16]. *N*-methyl-cyclo-atalaphylline-A (**215**) (*Glycosmis parva*) exhibits anti-allergic activity [17]. Arbutin (**43**) (*Glycosmis pentaphylla*) has been observed for a reduction of α-amylase and α-glucosidase activity [18]. Glybomine B (**61**) (*Glycosmis pentaphylla*) shows inhibition of EBV-EA induction by TPA [19]. Citracridone-I (**53**) (*Glycosmis pentaphylla*) exhibits inhibition of tumor cell growth in HL-60 cell lines [20]. Sequinoside K (**44**) (*Glycosmi spentaphylla*) is observed for its hepatoprotective activity [21]. Markhamioside F (**46**) (*Glycosmis pentaphylla*) shows anti-eczematic activity [22]. Kokusagine (**57**) (*Glycosmis pentaphylla*) exhibits growth inhibition of *Leucoagaricus gongylophorus* [23]. Glycoborinine (**62**) (*Glycosmis*

pentaphylla, Glycosmis montana, Glycosmis arborea) has been studied for its antifeedant activity against *Spodoptera litura* [24]. Limonin (**218**) (*Glycosmis parva*) shows cytotoxic activity against Caco-2, CEM/ADR5000 and CCRF-CEM leukaemia cells [25]. Limonexic acid (**219**) (*Glycosmis parva*) exhibits antinociceptive activity [26]. β-sitosterol (**71**) (*Glycosmis pentaphylla*) has been studied for its anti-inflammatory activity, apoptosis induction, hypocholesterolemic activity, angiogenic effect, anthelminthic and antimutagenic and immunomodulatory activities [27]. Oxyresveratrol (**74**) (*Glycosmis pentaphylla*) exhibits protein kinase C inhibition, antioxidant activity, neuroprotective activity, protective function of hepatic damage, hypoglycemic, antiviral and antibacterial activities [28]. 3-Formylcarbazole (**76**) (*Glycosmis pentaphylla*) and 3-methylcarbazole (**80**) (*Glycosmis pentaphylla*, *Glycosmis arborea*) are observed to have anti-TB activity [29]. Carbazole (**79**) *(Glycosmis pentaphylla)* derivatives exhibit antibacterial activity [30]. 5-Hydroxy-noracronycine (**208**) (*Glycosmis trichanthera*) has been observed for its anti-malarial activity [31]. N-methyl-atalaphylline (**209**) (*Glycosmis trichanthera*) is studied for inhibition of HL-60 cell growth [32]. Trichanthin-B (**203**) (*Glycosmis trichanthera*) exhibits moderate antifungal activity [33]. Sakambullin (**98**) (*Glycosmis pentaphylla, Glycosmis pseudoracemosa*) and methylgerambullin (**205**) (*Glycosmis trichanthera*) have been analyzed for their antitrypanosomal activities [34]. Glybomine A (**190**) and Glybomine C (**191**) (*Glycosmis arborea*) exhibit the inhibition of EBV-EA induction by TPA [19]. Glycrophylamine (**123**) (*Glycosmis arborea*) is observed for its cytotoxic activity against NC1-H187 cancer cells [35]. Phytoconstituents of *Glycosmis pentaphylla* have also been reported to inhibit protein kinase C [36]. 8-Prenylnaringenin (**104**) (*Glycosmis chlorosperma*) is used as a phytoestrogen for dietary supplement [37]. Mundulea-flavanone B (**105**) (*Glycosmis chlorosperma*) is observed for its antimutagenicity [38]. Z-bogorin (**109**) (*Glycosmis chlorosperma*) exhibits antifungal activity [39]. Glycozolinine (**193**) (*Glycosmis arborea*) is observed for its antituberculosis activity [40]. 5, 7-dihydroxy-2- [4-hydroxy-3-(methoxymethyl) phenyl]-6-C-β-D-glucopyranosyl flavone (**186**) (*Glycosmis arborea*) has been studied for its antibacterial activity [24]. 4′-O-Methylbonannione (**117**) (*Glycosmis pseudoracemosa*) shows cytotoxic activity against A2780 human ovarian cell line [41]. 5-O-Methylglovanon (**119**) (*Glycosmis craibii*) exhibits anti-bacterial activity [42]. (Z)-methyldambullin (**171**), (E)-Dambullin (**168**), (E)-methyldambullin (**170**) and (Z)-Dambullin (**169**) (*Glycosmis citrifolia*) are observed for their cytotoxic activity against T-lymphoblastic leukeamia cell line (CEM-SS) [43]. Glycocitrine-IV (**176**) (*Glycosmis citrifolia*) exhibits anti *Plasmodium falciparum* activity [44]. γ-Fagarine [33] (*Glycosmis pentaphylla, Glycosmis cochinchinensis, Glycosmis citrifolia, Glycosmis trichanthera*) and kokusaginine (**132**) (*Glycosmis bilocularis, Glycosmis cochinchinensis*) have been analyzed for their anti-gram positive bacteria activity [45]. Skimianine (**127**) (*Glycosmis macrophylla, Glycosmis arborea*) exhibits anticholinesterase activity [46]. Niranin (**147**) (*Glycosmis mauritiana*) has been observed to show antifungal and insecticidal activities [13]. Des-N-methyl noracronycine (**131**) (*Glycosmis cochinchinensis*) is analyzed for its antiproliferative activity against A-549, B-16 melanoma 4A5, CCRF-HSB-2 and TGBC11TKB cell lines [47]. Carbalexine A (**1**) (*Glycosmis pentaphylla, Glycosmis montana*) and carbalexine C (**3**) (*Glycosmis pentaphylla, Glycosmis montana*) have been observed for their cytotoxic activities against the human leukaemia cell line CCRF-CEM [48]. Lupeol (**8**) (*Glycosmis pentaphylla*) shows anti-cancer activity against cell lines including T-lymphoblastic leukemia CEM, breast carcinoma MCF-7, lung carcinoma A-549, multiple myeloma RPMI 8226, cervical carcinoma HeLa, malignant melanoma G361 after treatment for 72 h and it also inhibits proliferation of the ERα-negative breast cancer cells MDA-MB-231 [49]. Chrysin (**9**) (*Glycosmis pentaphylla*) induce apoptosis in U937, HL-60 and L1210 leukemia cells [50]. Epioleanolic acid (**6**) (*Glycosmis pentaphylla*) shows cytotoxic activity against various human tumor cell lines [51]. β-Amyrin (**7**) (*Glycosmis pentaphylla*) exhibits antifungal and antimicrobial activities [52]. Quercetin (**10**) (*Glycosmis pentaphylla*) has been observed for its antioxidant, hepatoprotective, antibacterial, anti-inflammatory and antiviral activities; Quercetin exhibits anticancer activity by acting on the G2-Mphase of the cell cycle and has shown antiviral activities [53]. Kaempferol (**11**) (*Glycosmis pentaphylla*) is observed as a growth regulator and its antiviral activity has also been recognised [53]. Spinasterol (**5**) (*Glycosmis pentaphylla*) acts as a gene expression modulator [54]. Guaiol (**84**) (*Glycosmis pentaphylla*) exhibits mosquito repellant activity [55]. Caryophyllene oxide (**14**) (*Glycosmis pentaphylla*) has been observed for *Anopheles gambiae* repellant action and anti-inflammatory activity [56]. Adamantane (**19**) (*Glycosmis pentaphylla*) derivatives exhibit antiviral activity [57]. β-Pinene (**21**) (*Glycosmis pentaphylla*) has been observed for antifungal activity [58]. Chlorospermine A (**86**) (*Glycosmis chlorosperma*) exhibits DYRK1A (Dual-specificity tyrosinephosphorylation-regulated kinase 1A)-inhibiting activity [59].

4. PHARMACOLOGY

4.1. Hepatoprotective Activity

The leaf and stem bark extracts of *Glycosmis pentaphylla,* exhibit a moderate dose-dependent protective effect in Swiss albino rats with CCl_4 induced hepatic damage, resulting in lowering of serum enzyme concentrations, which are augmented due to toxicity at a dosage of 750 mg extracts/kg body weight [60]. Also, the hepatoprotective activity of *Glycosmis pentaphylla* for liver damage induced by paracetamol has been reported [61]. The hepatoprotective effect of stem bark of *Glycosmis pentaphylla* against the CCl_4 induced jaundice in rats has also been reported. In the study, rats were administered with crude extract which was analyzed for levels of serum liver enzymes such as alanine transaminase [ALT], aspartate aminotransferase [AST], glutamyl transpeptidase [GGT] and total bilirubin. The observations revealed that the crude extract of *Glycosmis pentaphylla* can prevent hepatic injury/liver necrosis [62]. In another study, the butanolic extract from Ariel parts of *Glycosmis arborea* was observed to possess hepatoprotective effects [63].

4.2. Antimicrobial Activity

The extracts from the stem, leaf and root parts of *Glycosmis pentaphylla* were obtained using different solvents

viz., petroleum ether, methanol, and acetone, exhibiting inhibitory effects at varying degrees against bacterial growth. Methanolic extracts from stem and leaf have shown antibacterial effect on *Bacilllus subtilis* at concentrations of 50% and 100% [12-16 mm inhibitory zone]. Also, the methanolic extract from stem has shown better inhibitory effect [14-15 mm inhibitory zone] against *Escherichia coli* as compared to other parts and solvents used [64]. In another study, the methanolic extracts from leaves and stems of *Glycosmis pentaphylla* showed considerable antimicrobial activity against *Escherichia coli* with the zone of inhibition 23.67 mm [as 400 µg extract per disc was used]. Significant inhibition of bacterial growth was also observed against *Salmonella paratyphi* indicating the presence of potential antibacterial agents [65]. A recent study showed that a flavone C-glycoside exhibits antimicrobial activity against bacterial plant pathogens including *Agrobacterium tumefaciens, Pectobacterium carotovorum,* and *Pseudomonas syringae.* Also, inhibitory activities against *Agrobacterium tumefaciens* and *Pectobacterium carotovorum* were observed at moderate levels at a concentration of 200 µg, and fatal concentration for *Pseudomonas syringae* was found to be 500 µg [24]. Similarly kokusaginine, a compound isolated from the twigs of *Glycosmis cochinchinensis* exhibited antibacterial activity against methicillin-resistant *Staphylococcus aureus* SK1 at a moderate level, with MIC value of 16 mg/ml [66]. Another study showed that the methanolic extract of *Glycosmis pentaphylla* exhibits maximum antibacterial activity against *Klebisella aerogens, Staphylococcus aureus, Streptococci,* and *Escherichia coli* [67].

Similar studies for antifungal activity of extracts from *Glycosmis pentaphylla* have been performed and it was observed that methanolic extract at 50 and 100% concentrations showed an inhibitory effect against the growth of the fungus, *Mucor sp*. [65]. Amides isolated from lipophilic leaf extracts of *Glycosmis cyanocarpa, Glycosmis mauritiana,* and *Glycosmis crassifolia* displayed pronounced antifungal activity against *Cladosporium herbarum* [13]. Another study shows that out of petroleum ether, chloroform and methanol extract of *Glycosmis pentaphylla*, methanolic extract exhibits maximum antifungal activity against *Candida ablicans* and *Aspergillus niger* [67]. Bioassay-guided TLC analysis of crude leaf extract of *Glycosmis cyunocarpa* using a spore suspension of *Cladosporium cladosporioide* showed two clearly visible inhibition zones, indicating the presence of fungitoxic compounds [13]. Two substances [sinharine and methylsinharine] with antifungal activity were isolated from $CHCl_3$, fraction of the methanolic leaf extract of *Glycosmis cyanocarpa* [68].

4.3. Cytotoxicity, Anticancer and Apoptosis-inducing Effect

Compounds extracted using chloroform from *Glycosmis citrifolia* and *Glycosmis elongate* were analyzed for cytotoxic activity against T-lymphoblastic leukeamia cell line [CEM-SS]. Amides [E]-dambullin, [Z]-dambullin and mixture of methyldambullin [[E] - and [Z]-conformer], exhibited strong activity with IC_{50} values of 1.6, 2.2, 3.0 µg/ml, respectively. For the antioxidant activity using the DPPH free radical, none of the compounds were observed to display significant activity except for the mixture of the two methyldambullin conformers which showed moderate activity having 208.3 µg/ml IC_{50} value. Compared with the activity of vitamin C [IC_{50} = 14.3 µg/ml] and quarcetin [IC_{50} = 78.5 µg/ml], the scavenging activity of the compounds mixture was much weaker [43]. In another study, the compounds isolated from the roots and twigs of *Glycosmis macrophylla* were evaluated for cytotoxicity against NCI-H187 cancer cell line using the colorimetric method. The observations showed that glycozoline and dehydrothalebanin B were found to be weakly active with the IC_{50} values of 47.94 and 46.23 mg/ml, respectively. Ellipticine and doxorubicin were used as reference substances having respective IC_{50} values of 1.06 and 0.087 mg/ml [69]. Another study showed that alkaloids isolated from the twigs and leaves of *Glycosmis montana* exhibited cytotoxic activity that was against the human leukaemia cell line CCRF-CEM as analysed by growth inhibition assay [48]. The lethality of the methanolic extracts from stems and leaves of *Glycosmis pentaphylla* was evaluated in *Artemia salina* using brine shrimp lethality bioassay. The LC_{50} was found to be 5.51, 47.63 and 2.81 µg/ml for stems, leaves, and vincristine sulfate respectively. In comparison with vincristine sulfate, the cytotoxicity exhibited by the methanolic extracts of stems of *Glycosmis pentaphylla* was highly potent whereas the activity of the methanolic leaf extracts was observed to be significant. Arborinine, an acridone alkaloid obtained from *Glycosmis pentaphylla*, exhibited significant inhibition of crown gall tumors produced by *Agrobacterium tumefaciens* in a potato disc bioassay [65]. Chloroform extracts of stem bark, leaf, roots and stem wood of *Glycosmis pentaphylla* were analysed against the brine shrimp, *Artemia salina* nauplii for cytotoxic activity, for which dose-mortality assay produced LC_{50} values of 28.579, 28.659, 57.213 and 84.111 ppm, respectively [70].

Another study investigated the effect of *Glycosmis parva* leaves on human colorectal cancer. It was observed that ethyl acetate extracts were cytotoxic to HT29 in a dose-dependent manner having IC_{50} values of 69.50, 55.86, and 49.04 µg/ml at 24, 48, and 72 h, respectively. Extract at 50–100 µg/ml significantly induced HT29 apoptosis. At concentrationsI of 25–100 µg/ml, it inhibited HT29 cell proliferation in dose-dependent manner and at 100 µg/ml, it caused G2M accumulation resulting in a change of Bcl-2 family protein expression. It also resulted in a decrease of COX2 expression at 25–100 µg/ml concentrations. The study concluded that ethyl acetate extract from the leaves of *Glycosmis parva* exhibited cytotoxic activity along with apoptosis induction, cell proliferation inhibition and cell cycle arrest in HT29 cells [71, 72]. The underlying mechanism may involve a decrease in COX2 expression and changes in expression levels of Bcl-2 family proteins which favor cancer cell death [71]. Another study showed that arborinine, an acridone alkaloid obtained from *Glycosmis pentaphylla*, exhibited significant crown gall tumor inhibition produced by *Agrobacterium tumefaciens* in a potato disc bioassay [73]. A similar study showed that alkaloids obtained from acetone extract from stems of *Glycosmis arborea* exhibited their inhibitory effects on induction of Epstein-Barr Virus Early Antigen [EBV-EA] through tumor promoter 12-O-tetradecanoylphorbol-13-acetate [TPA] [34].

The study evaluated *in vitro* anticancer and apoptosis activity induced by *Glycosmis pentaphylla* in hepatocellular carcinoma cell line [Hep3B] [74]. This study concluded that

Table 1. Overview of phytoconstituents present in *Glycosmis* species.

Plant Part	Category	Constituents	References
Glycosmis pentaphylla			
Leaf	Carbazole Alkaloids	Carbalexin A (**1**); Carbalexin B (**2**); Carbalexin C (**3**).	[88]
		Mupamine (**4**).	[89]
	Sterol	Spinasterol (**5**)	[90]
	Triterpenoids	Epioleanolic acid (**6**)	
		beta-Amyrin (**7**)	
		Lupeol (**8**)	[75]
	Flavonoids	Chrysin (**9**); Quercetin (**10**); Kaempferol (**11**).	
	Essential Oils	Bicyclo[6.1.0]non-1-ene (**12**); Benzaldehydeoxime (**13**); Caryophyllene Oxide (**14**); 3,4-dimethyl-2-prop-2-enyl-2,5-dihydrothiophene 1,1-dioxide (**15**); Bicyclo[5.1.0]octane (**16**); 1,4-Dimethyl-8-isopropylidenetricyclo[5.3.0.0(4,10)]decane (**17**); 2-Methoxy-3H-azepine (**18**); Adamantane (**19**); βPanasinsene (**20**); β Pinene (**21**).	[91]
	Quinazolone Alkaloids	Arborine (**22**).	[92]
		Glycosmicine (**23**); Glycorine (**24**); Arborine (**22**); Glycosminine (**25**); Glycophymine (**26**); Glycophymoline (**27**); Glycosine (**28**); 1-Methyl-3-(2-phenylethyl)quinazoline-2,4(1H,3H)-diones (**233**).	[93]
		Glycolone (**29**).	[94]
Fruit	Hydroperoxy-quinolone Alkaloids	Glycopentaphyllone (**30**); Acutifolin A (**197**); 3-(3',3'-Dimethylallyl)-4,8-dimethoxy-N-methyl-Quinolin-2-one (**184**); Glycocitlone C (**31**); Arborine (**22**); Dictamine (**32**); Ɣ-Fagarine (**33**); Skimmianine (**56**); 1-Hydroxy-3,4-dimethoxy-10-methylacridan-9-one (**34**); Arborinine (**54**).	[9]
Stem	Hydroquinone Diglycosides	Glypentoside A (**35**); Glypentoside B (**36**); Glypentoside C (**37**); Seguinoside F (**39**).	[95]
	Phenolic Glycosides	Glycopentoside A (**38**); Glycopentoside B (**40**); Glycopentoside C (**41**); threo-1-C-syringylglycerol 4-O-b-D-glucopyranoside (**42**); Arbutin (**43**); Sequinoside K (**44**); Syringin (**45**); Markhamioside F (**46**); Tachioside (**47**); Icariside E5 (**48**);	[96]
	Naphthoquinone	Glycoquinone (**49**).	[97]
	Acridone Alkaloids	Glycocitrine-III (**50**); Noracronycine (**51**); des-N-methylnoracryonycine (**131**); des-N-methylacronycine (**52**); Citracridone-I (**53**); Arborinine (**54**); 5-Hydroxyarborinine (**224**); Acrifoline (**55**).	
	Furoquinoline Alkaloids	Kokusagine (**57**).	
	Carbazole Alkaloids	4-(7-Hydroxy-3-methoxy-6-methyl-9H-carbazol-4-yl)but-3-en-2-one (**58**); Bisglybomine B (**59**); Biscarbalexine A (**60**); Glybomine B (**61**); Glycoborinine (**62**); Carbalexine A (**1**); 4,8-Dimethoxy-1-methyl-3-(3-methylbut-2-en-1-yl)quinolin-2(1H)-one (**63**); 4,8- dimethoxyfuro[2,3-b]quinolone; Skimmianine (**56**); Arborinine (**54**).	[98]
	Isoflavones	3',7-Dihydroxy-4',5,6-trimethoxyisoflavone 7-*O*-(5-*O*-*trans*-*p*-coumaroyl)-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside; 2',7-Dihydroxy-4',5',5,6-tetramethoxyisoflavone 7-*O*-(5-*O*-*transp*-coumaroyl)-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside; 2',7-Dihydroxy-4',5',5,6-tetramethoxyisoflavone 7-*O*-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside; 7-Hydroxy-4',8-dimethoxyisoflavone 7-*O*-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside; 7-Hydroxy-4',6-dimethoxyisoflavone 7-*O*-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside; 4',5-Dihydroxy-3',7-dimethoxyisoflavone 4'-*O*-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside (**64**); 7-Hydroxy-4'-methoxyisoflavone 7-*O*-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside (**65**); Coromandelin (**66**); 4',5-Dihydroxy-6,7-dimethoxyisoflavone 4'-*O*-*α*-D- apiofuranosyl-(1->6)-*α*- D-glucopyranoside (**67**); Tectorigenin 7-*O*-*α*-D-apiofuranosyl-(1->6)-*α*-D-glucopyranoside (**232**).	[99]

(Table 1) contd….

Plant Part	Category	Constituents	References
	Flavanols	Glycoflavanones A (**68**); Glycoflavanones B (**69**); 4'-O-methylgallocatechine (**70**); β-sitosterol (**71**); Alphitol (**72**); 3,4-Dimethoxy-5-hydroxy-trans-cinnamyl alcohol (**73**); Oxyresveratrol (**74**).	[100]
Root & Root Bark	Carbazole Alkaloids	Glycozolicine (**75**); 3-Formyl carbazole (**76**); Glycosinine (**77**).	[101]
		Glycozolidol (**78**).	[102]
	Alkaloids	Carbazole (**79**); 3-methylcarbazole (**80**)	[103]
	Sterol	Stimast-5-en3-yl-9-octadecenoate; gamma-Sitosterol (**81**),	[83]
	Furocoumarin Derivative	Marmesin (**82**)	
	Alcohols, Amines & Acids	5-Hydroxypipecolic acid (**83**), Guaiol (**84**), 1H-Indole-3-ethanamine (**85**),	
Glycosmis parviflora			
Leaf	Carbazole Alkaloids	carbalexine A (**1**); carbalexine B (**2**); carbalexine C (**3**).	[88]
Glycosmis chlorosperma			
Stem bark	Alkaloids	Chlorospermine A (**86**); Chlorospermine B (**87**); Atalaphyllidine (**88**); Acrifoline (**89**);	[59]
Leaf	Prenylatedsulfonyl amides	Gerambullol (**90**); Gerambullin (**91**); β-Hydroxy-gerambulin (**92**); β-Hyroxy-gerambullol (**93**); β-Hyroxy-gerambullal (**94**); Sakerinol A (**95**); O-Methylsakerinol A (**96**); Sakerinol B (**97**); Sakambullin (**98**); O-Methylsakambullin (**99**); Dambullin (**100**); Sakerine (**101**).	[104]
	Prenylatedflavanones and flavanonols	Selinon (**102**); 7-O-Methylselinon (**103**); 8-Prenylnaringenin (**104**); Mundulea-flavanone B (**105**); 4´-O-Methyl-8-prenylnaringenin (**106**); Flowerine (**107**); Chlorospermin (**108**).	[105]
	Quinazolone Derivatives	(Z)-Bogorin (**109**); (E)-Bogorin (**110**); (Z)-3,4-Dihydro-3-(2-phenylethenyl)-quinazolin-4-one.	[106]
	Sulphur Containing Amides	Penimide B (**111**); Penimide A (**112**); Penangin (**113**); Isopenangin (**114**).	[107]
	Sulfonyl Amides	Gerambullol (**90**), B-Hydroxygerambullin (**92**); β-Hydroxygerambullol (**93**); β-Hydroxygerambullal (**94**); Sakerinol A (**95**); O-Methylsakerinol A (**96**); Sakambullin (**98**); O-Methylsakambullin(**99**).	[104]
Glycosmis pseudoracemosa			
Leaf	Prenylatedsulfonyl Amides	Gerambullol (**90**); Gerambullin (**91**); β-HyroxyGerambulin (**92**); β –HyroxyGerambullol (**93**); β –HyroxyGerambullal (**94**); Sakerinol A (**95**); O-Methylsakerinol A (**96**); Sakerinol B (**97**); Sakambullin (**98**); O-Methylsakambullin (**99**); Dambullin (**100**); Sakerine (**101**).	[104]
	Prenylated Flavanones and flavanonols	Puyanol (**115**); Puyanin (**116**); 4´-O-Methylbonannione (**117**).	[105]
	Sulfonyl Amides	Sakerinol B (**97**).	[104]
Glycosmis craibii			
Leaf	Prenylated Flavanones and flavanonols	Glovanon (**118**); 5-O-Methylglovanon (**119**).	[105]
Glycosmis puberula			
Leaf	Prenylated Flavanones and flavanonols	Mepuberin (**120**); Glypuberol (**121**).	[105]
Glycosmis sapindoides			
Leaf	Prenylated Flavanones and flavanonols	Glysapinol (**122**).	[105]

(Table 1) contd….

Plant Part	Category	Constituents	References
Glycosmis macrophylla			
Roots and Twigs	Carbazole Alkaloid	Glycrophylamine (**123**); Glycrophylamide (**124**); 2-Methoxy-3-methylcarbazole (**125**); Glycozoline (**126**); Skimianine (**127**); Dehydrothalebanin B (**128**).	[69]
Glycosmis cochinchinensis			
Twigs	Alkaloids	Glycosmisacridone (**129**); Glycosmisindole (**130**); des-N-methylnoracronycine (**131**); Noracronycine (**51**); Atalaphyllidine (**88**); 1-hydroxy-3,4-dimethoxy-10-methylacridan-9-one (**34**); γ-fagarine (**33**); Skimmianine (**56**); Kokusaginine (**132**); Integriquinolone (**133**).	[108]
Leaves	Quinazoline Alkaloids	Glycozolone-A (**134**); Glycozolone-B (**135**);	[109]
	Anthranilylamide	Glycoamide-A (**136**); Glycoamide-B (**137**).	
Glycosmis Montana			
Twigs and leaves	Indole Alkaloids	(E)-3-(3-hydroxymethyl-2-butenyl)-7-(3-methyl-2-butenyl)-1H-indole (**138**).	[48]
	Carbazole Alkaloids	Glybomine B (**61**); Glycoborinine (**62**); Carbalexine B (**2**); Carbalexine A (**1**); Carbalexine C (**3**); 2-Hydroxy-3-methyl-9H-carbazole (**139**).	
	Sulfur-containing Flavanols	Glymontanine A (**140**); 4'-O-methylgallocatechin (**70**); Glymontanine B (**141**).	[110]
	Flavanol Dimers	Montahomobisflavan A (**142**); Montahomobisflavan B (**143**).	
Glycosmis mauritiana			
Root	Flavone Glucosides	Luteolin 8-C-*β*-D-glucopyranoside (**144**).	[111]
	Alkaloids	1-Hydroxy-3-methoxy-2-(3-methylbut-2-enyl)-*N*-methylacridan-9-one (**145**); 4,8-Dimethoxy-3-(3-methylbut-2-enyl)-*N*-methyl-2-quinolone (**146**).	[112]
Leaf	Amides	Niranin (**147**).	[13]
	Sulphur-containing Amides	Methylillukumbin B (**148**); Illukumbin B (**149**); Methylillukumbin A (**150**).	[107]
Aerial parts	Quinolinone Alkaloids	7, 8-Dimethoxy-2,2,6-trimethyl-pyrano quinolin-5-one (**151**); 4-Methoxy 1-methyl quinolin-2-one (**152**);	[113]
	Acridone Alkaloids	1-Hydroxy-10-methyl acridone (**153**); 1-Hydroxy-2, 3-dimethoxy-10-methylacridin-9-one (**154**).	
	Flavone Glycoside	Luteolin-4'-O-[α-L-rhamnopyranosyl-(1→2)-{α-L-rhamnopyra-nosyl-(1→6)}-β-D-glycopyranoside].	
Stem Bark	Acridone Alkaloids	Noracronycine (**51**); des-N-methylacronycine (**52**).	[114]
	Carbazole Alkaloids	Glycomaurin (**155**); Glycomaurrol (**156**),	
Glycosmis citrifolia			
Leaf	Flavonoids	Glychalcone-A (**157**); Glychalcone-B (**158**), Glyflavanone-A (**159**); Glyflavanone-B (**160**).	[115]
	Amido-sulphoxides	Glycothiomin-A (**161**), Glycothiomin-B (**162**).	
	2-Quinolone Alkaloid	Glycocitridine (**163**); ϒ-Fagarine (**33**); Skimmianine (**56**); 1,2-Dimethyl-4(1H)-quinolone (**164**); Evomeliaefolin (**165**).	
	Furopyridine Alkaloids	(Z)-Rhoifolic acid methyl ester; (E)-Rhoifolic acid methyl ester; Chlorophylls methyl-21-hydroxy-(21R)-pheophorbide-A; Methyl-21-hydroxy-(21R)-pheophorbide-B; Amidosulphidepenangin (**166**).	
	Triterpene	5(**6**)-Glutene-3α-ol (**167**).	[43]
	Sulphur-containing Amides	(E)-Dambullin (**168**); (Z)-Dambullin (**169**); (E)-methyldambullin (**170**); (Z)-methyldambullin (**171**).	
Root	Acridone Dimers	Glycobismine-F (**172**); Glycobismine-G (**173**); Glycobismine-D (**174**); Glycobismines-E (**175**); Glycocitrine–IV (**176**); Glycocitrine-VI (**177**).	[116]

(Table 1) contd….

Plant Part	Category	Constituents	References
Root & Stem Bark	Acridone Alkaloid	Glycobismine-D (**174**); Glycobismine-E (**175**); Glycocitrine-IV (**176**); Glycocitrine-V (**178**); Glycocitrine-VI (**177**).	[117]
	Quinolone Alkaloid	Glycocitlone-A (**179**); Glycocitlone-B (**180**); Glycocitlone-C (**181**).	
Glycosmis arborea			
Overground Part	Tetracyclic Triterpene Alcohols	(24S)-24-Methyl-5α-lanosta-9(**11**),25-dien-3β-ol (**182**); 24,24-Dimethyl-5α-lanosta-9(**11**),25-dien-3β-ol (**183**); (24S)-24-Methyl-5α-lanosta-9(**11**),25-dien-3α-ol; 24,24-Dimethyl -5α-lanosta-9(**11**),25-dien-3α-ol.	[118]
	Acid	Glycoric acid	[119]
Root	Carbazole Alkaloids	Glycoborinine (**62**); Glycozoline (**126**); Glycozolidine (**195**); Skimmianine (**56**); 3-(3',3'-Dimethylallyl)-4,8-dimethoxy-N-methyl-Quinolin-2-one (**184**).	[120]
Leaf	C-glycosyl Flavone	7,4'-dihydroxy-5-methoxyflavone-6-C-b-D-glucopyranoside (**185**).	[121]
	Flavanoids	5,7-dihydroxy-2-[4-hydroxy-3-(methoxymethyl)phenyl]-6-C-β-D-glucopyranosyl flavone (**186**); 5,7,4'-Trihydroxy-3'-methoxy flavones (**187**); 5,5'-Dihydroxy-4'-methoxy-7-O-β-D-glucupyranosylFlavanone (**188**); 5,5'-Dihydroxy-4'-methoxy-7-O-(L-rhamnosyl-(1‴→6‴)-β-D-glucopyranosyl) flavanone (**189**).	[122]
Stem	Carbazole Alkaloids	Glybomine A (**190**); Glybomine B (**61**); Glybomine C (**191**); 3-Methylcarbazole (**80**); Methyl carbazole-3-carboxylate (**192**); Glycozolinine (**193**); Glycoborinine (**62**); Glycozoline (**126**); 5-Methoxy-3-methylcarbazole (**194**); Glycozolidine (**195**); Glycomaurrol (**156**).	[19]
	Furoquinoline Alkaloids	Skimianine (**127**); 4,8-dimethoxyfuro[2,3-*b*]quinolone (**196**).	
	2-Quinolone Alkaloids	Glycocitlone C (**31**); Acutifolin A (**197**); 4,8-Dimethoxy-3-(3-methylbut-2-enyl)-*N*-methyl-2-quinolone (**198**).	
	4-Quinolone Alkaloids	Isodictamnine (**199**); Iso-*γ*-fagarine (**200**).	
	Acridone Alkaloids	1-Hydroxy-3-methoxy-10-methylacridan-9-one (**201**); Arborinine (**54**).	
	Quinazoline Alkaloids	Arborine (**22**).	
Glycosmis trichanthera			
Leaf	Sulphur-containing amides	Trichanthin-A (**202**); Trichanthin-B (**203**); Glyparvin-A (**204**); Methylgerambullin (**205**).	[123]
Stem Bark	Prenylatedacridone Alkaloids	Yukocitrin (**206**); Junosin (**207**); 5-Hydroxy-noracronycine (**208**); N-methyl-atalaphylline (**209**); N-methyl-atalaphyllinine (**210**).	
Root Bark	Quinoline Alkaloids	Skimmianine (**56**); ϒ-Fagarine (**33**); des-N-methyl-noracronycine (**131**); N-methylatanine (**211**); 3,7-Diprenylated indole.	
Glycosmis petelotii			
Leaf	sulphur-containing Indole Alkaloid	Glypetelotine (**212**)	[124]
Glycosmis elongate			
Leaf	Alkaloids	Skimmianine (**56**); Arborinine (**54**).	[43]
Glycosmis stenocarpa			
Root	Dimericpyranocarba-zole Alkaloids	bis-Isomahanine (**213**).	[125]
Glycosmis parva			
Branch & Leaf	Acridone Alkaloids	Glycosparvarine (**214**); *N*-methyl-atalaphylline (**209**); *N*-methyl-cyclo-atalaphylline-A (**215**); Glycofolinine (**216**); Citramine (**217**); Arborinine (**54**).	[15]
	Limonoids	Limonin (**218**); Limonexic acid (**219**); Isolimonexic acid (**220**).	
	Sulfur-containing Propanamide Derivatives	*S*-deoxy-dihydro-glyparvin (**221**); *S*-deoxy-tetrahydro-glyparvin (**222**); Glyparvin-A (**204**); Dihydroglyparvin (**223**).	

(Table 1) contd….

Plant Part	Category	Constituents	References
Glycosmis bilocularis			
Stem	Alkaloids	5-Hydroxy-arborinine (**224**).	[126]
Leaf	Alkaloids	Skimmianine (**56**); Kokusaginine (**132**); 5-Hydroxy-arborinine (**224**); Dictamnine (**225**).	[126]
		Arborine (**22**); Arborinine (**54**); Glycarpine (**226**); Kokusaginine (**132**); Skimmianine (**56**); 5-Hydroxy-arborinine (**224**).	[127]
Glycosmis crassifolia			
Leaf	Amides	Thalebanin B (**227**); Dehydrothalebanin B (**128**); Dehydrothalebanin A (**228**).	[13]
Glycosmis cyanocarpa			
Leaf	Amides	Dehydroniranin B (**229**); Dehydroniranin A (**230**).	[13]
	Alkaloids	Glycarpine (**226**); Evolitrine (**231**).	[128]

active molecules in the ethanol extract of *Glycosmis pentaphylla* were flavonoids/quercetin which induce apoptosis on cancer cell line, Hep3 B, by decreasing p53 expression and increasing the expression ratio of Bax/Bcl2 genes in a manner which is both time and dose-dependent [75]. Another study showed that the extracts and fractions of leaves of *Glycosmis pentaphylla* possess specific cytotoxicity towards breast cancer cells. The selected fractions of dichloromethane and ethanol were able to arrest the cell cycle and induce apoptosis in MCF-7 and MDA-MB-231 breast cancer cells through the activation of caspase-3/7. HPLC analysis of selected fractions from petroleum ether extract indicated the presence of kaempferol, which induces apoptosis in MCF-7cells, and chrysin, which induces apoptosis in cancer cells and inhibits metastasis in triple negative breast cancer cells. HPTLC analysis of a fraction of petroleum ether indicated the presence of lupeol which exhibits known anticancer activity against MCF-7 cells [75].

4.4. Antioxidant Property

A study was conducted to investigate the antioxidant effects of different crude extracts [ethanolic, petroleum ether and aqueous] of the plant *Glycosmis pentaphylla.* The antioxidant activity was analyzed by using antioxidant assays including nitric oxide, 2, 2'-azino-bis [3-ethylbenzthiazoline-6-sulfonic acid] [ABTS], 1,1-diphenyl-2-picrylhydrazyl [DPPH] and hydrogen peroxide [H_2O_2] scavenging method. DPPH assay revealed that extracts of *Glycosmis pentaphylla* have the ability to scavenge free radicals. Antioxidant activity of the ethanolic extract of *Glycosmis pentaphylla* was revealed using ABTS assay with the maximum IC_{50} value being 26.2 µg/ml, suggesting its free radical scavenging activity. Nitric oxide and H_2O_2 scavenging method also revealed the antioxidant activity of ethanolic extract of *Glycosmis pentaphylla* [76]. The aqueous and methanolic extracts of roots showed antioxidant activity which indicates the presence of polyphenolic compounds in the extracts [77].

4.5. Antipyretic, Analgesic and Anti-nociceptive Activity

A study on ethanolic extracts of *Glycosmis pentaphylla* exhibited noteworthy antipyretic activities in pyrexia induced by Brewer's yeast in rats. The maximum antipyretic activity was produced by ethanolic extract of plant *Glycosmis pentaphylla* [200 mg/kg]. Basically, non-steroidal anti-inflammatory drugs generate antipyretic action by the inhibition of prostaglandin synthetase within the hypothalamus. Hence, the antipyretic activity of *Glycosmis pentaphylla* is probably by the inhibition of prostaglandin synthesis in the hypothalamus [78]. Another study on Swiss albino mice evaluated an ethanolic extract for anti-hyperglycemic and analgesic effects. Observations showed an anti-hyperglycemic effect with blood sugar reduction which was more significant at 2 hours, as compared to that induced by metformin. Another study indicated that the extract has anti-hyperglycemic effect in both 1 day and 7-day duration, which can be compared to metformin HCL, which is a known and widely used anti-hyperglycemic agent. The *Glycosmis pentaphylla* extract also exhibited an analgesic effect which is comparable to known analgesic drug diclofenac sodium [79]. In a similar study, a methanolic leaf extract was investigated for its anti-nociceptive activity. The *Glycosmis pentaphylla* extract produced an anti-nociceptive effect with late phase formalin-induced pain inhibition and lowering in the number of writhing in comparison with the control group [$P<0.05$] in writing test. The antinociceptive activity of the extract at dosage levels of 200mg/kg body weight was comparable to that of indomethacin 5mg/kg and less than that of morphine 1mg/kg, while at 400mg/kg, it was more than that of selected standards. The significant antinociceptive activity of the extract can be attributed to its involvement in prostaglandin biosynthesis [80].

4.6. Antidiabetic and Anti-arthritic Activity

The Anti-diabetic potential of the ethanolic extract of stem bark of *Glycosmis pentaphylla* was evaluated by the streptozotocin induced diabetic model. Significant [$p\leq0.01$] reductions in fasting blood glucose levels and increase in serum insulin levels were observed in diabetic animals due to pancreatic β cell regeneration. The extract was found to be non-toxic and well tolerated after chronic oral administration. The study concluded that *Glycosmis pentaphylla* is safe and has strong anti-diabetic activity and efficacy [at doses of 400-800 mg/kg] which are almost comparable to that of glybenclamide [81]. Another study showed that chloroform, ethyl acetate and ethanol extracts of *Glycosmis pentaphylla* roots are capable of controlling the production of auto-antigen involved in the inhibition of protein

denaturation. This study confirms the traditional claim of *Glycosmis pentaphylla* as an anti-arthritic drug [82]. In a similar study, anti-arthritic potential of the ethanolic extract from the stem bark of *Glycosmis pentaphylla* was evaluated by FCA induced arthritis model. Graded doses of the ethanolic extract of *Glycosmis pentaphylla* were administered to experimental arthritic and diabetic rats [different groups] for 21 days. A significant improvement of the haematological parameters like RBC count, Hb level, and the ESR to a near normal level was observed indicating the significant recovery from the anemic condition and arthritic progress thus justifying its noteworthy role in arthritic conditions. The study concluded that the extract of *Glycosmis pentaphylla* exerts potent anti-arthritic activity by significantly altering the pathogenesis during arthritic conditions without showing any side effect in case of FCA induced arthritis rats [81].

4.7. Insecticidal and Repellent Activity

The ethyl acetate fraction of *Glycosmis pentaphylla* leaf extract was observed to inhibit the juvenile hormone III-biosynthesis from the corpora allata of field cricket, *Gryllusbi maculatus*, in a dose dependent manner. This alkaloid, identified as arborine, was found to contain strong insecticidal activity against dipteran species as well as larvicidal activity against the mosquito [*Culex quinquefasciatus*] [83]. Another study proved that the leaf extract of *Glycosmis pentaphylla* effectively inhibits first instar larvae stage of the citrus leaf miner, *Phyllocnistis citrella* [Stainton]. Studies also revealed that oral administration of *Glycosmis. pentaphylla* ethyl acetate extract to the penultimate and final instar larvae of the castor semilooper, *Achaea janata*, reduced the weight gain and inhibited larval to pupal and pupal to adult metamorphosis, respectively [62]. Amides isolated from lipophilic leaf extracts of *Glycosmis mauritiana, Glycosmis cyanocarpa,* and *Glycosmis crassifolia* displayed insecticidal activity against neonate larvae of *Spodoptera littoralis*. It was mainly due to sulfur containing imide ritigalin [12]. In further studies, the larvicidal effect of *Glycosmis pentaphylla* has also been measured with larvae of *Diaprepes abbreviatus* after rearing them on roots of rutaceous seedlings for 35 to 42 days. Growth-inhibiting activity was found in both live and milled roots of *Glycosmis pentaphylla*. Milled root samples at 5% concentrations [w/v] were incorporated into a standard semi-defined diet and growth of larval weevils was recorded. The results from these studies showed that the roots of *Glycosmis pentaphylla* have growth inhibiting activity against *Diaprepes abbreviate* [62]. Chloroform extracts of leaves, stem bark, stem wood and root extracts of *Glycosmis pentaphylla* were tested for repellency against *Tribolium castaneum* adults where the root wood and root bark showed strong repellent activity [71].

The antihelmintic effect of methanolic leaf extract from *Glycosmis pentaphylla* was studied on adult Indian earthworm [*Pheritima posthuma*] and observed dose dependent, spontaneous motility [paralysis] inhibition and death. At higher concentrations [60 mg/ml], methanolic extract demonstrated paralysis as well as the death of worms. Saponins and tannins which may be present in the methanolic leaf extract of *Glycosmis pentaphylla* are responsible for antihelmintic effects by binding of tannins with free proteins in the gastrointestinal tract of the host animal and cause death [80].

4.8. Wound Healing Activity

In this study, *Glycosmis arborea* leaf extract significantly [$P < 0.05$] increased the percentage of wound contraction [96.91%] for topical application of ointment [10%] in excision wound model as compared to control [60.27%] and a decrease in the epithelization time. Rats treated with *Glycosmis arborea* extract [400 mg/kg] exhibited significant [$P < 0.05$] increase in hydroxyproline content at 54.94 ± 0.96 mg/gm as compared to control at 30.77 ± 1.13 mg/gm. These results demonstrated that *Glycosmis arborea* showed wound-healing properties by increasing the synthesis of collagen. Thus from this study, it is concluded that the *Glycosmis arborea* leaf extract has wound healing potential and hence justifies its application as folklore medicine in India [84].

4.9. Immunomodulatory Activity

During the studies, it was observed that on oral administration, ethanolic extract from leaves of *Glycosmis pentaphylla* showed a noteworthy increase in humoral antibody responses for 21 days, by elevating the haemagglutination antibody titer at doses of 100 and 200 mg/kg. A significant dose-dependent increase in the percentage of neutrophil adhesion was also observed. The study revealed that the ethanolic extract of *Glycosmis pentaphylla* holds promise to be used as an immunomodulatory agent, which acts by stimulating both the specific and nonspecific arms of immunity. Further studies using *in vivo* and *in vitro* models of immunomodulation are recommended to confirm the immunomodulatory activity of *Glycosmis pentaphylla* leaves and their mechanism of action [85].

4.10. Antiviral Activity

In this study, organic extracts of *Glycosmis parva* were subjected to tests for antiviral activity in assays for plaque reduction against HSV-1 and HSV-2. Hexane and ethyl acetate extracts from branches, and hexane extract from leaves displayed anti-herpes virus activities in the inactivation inhibition, while the ethyl acetate extract from leaves exhibited anti-herpes virus activities in both inactivation treatment and post-inhibition [15]. Another study showed that alkaloids isolated from the twigs and leaves of *Glycosmis montana* exhibited weak to moderate *in vitro* inhibitory activity against HIV replication in C8166 cell lines [48].

4.11. Membrane Stabilizing and Thrombolytic Activities

In vitro study on rat erythrocytes showed that the methanol extract from the leaves and stems of *Glycosmis arborea* and their petroleum ether, carbon tetrachloride, chloroform and aqueous soluble partitionates exhibited membrane stabilizing activity as they inhibit heat as well as hemolysis induced by hypotonic solution. The pet-ether soluble fraction of leaves and stems of *Glycosmis arborea* showed inhibition of RBC hemolysis caused by hypotonic solution and heat as compared to the standard acetyl salicylic acid at a concentration of 0.01 mg/ml, respectively. Also, the chloroform soluble fraction of crude methanol extract of

both the leaves and stems of *Glycosmis arborea* showed highest thrombolytic activity having clot lysis value of 36.50% while standard streptokinase and water used as positive and negative controls respectively, exhibited 64.25 ± 0.26 and 2.35 ± 0.35 % clot lysis, respectively, whereas the carbon tetrachloride and pet-ether soluble materials from stems of *Glycosmis arborea* displayed moderate thrombolytic activities [86].

4.12. Anti-Inflammatory Activity

The study evaluated anti-inflammatory effect of methanolic and ethyl acetate extracts of roots of *Glycosmis pentaphylla* in carrageenan induced albino Wistar rats. The anti-inflammatory effects of ethyl acetate extract of *Glycosmis pentaphylla* at 200, 400 mg/kg were found to be significant [P<0.001] in reducing rat paw oedema induced by carrageenan, whereas methanolic and ethyl acetate extracts showed a noteworthy reduction of paw oedema at 400mg/kg. For comparison, ibuprofen [50 mg/kg] served as the reference anti-inflammatory agent. Further studies are needed to explore the mechanism by which *Glycosmis pentaphylla* produces anti-inflammatory activity [87].

CONCLUSION

This review clearly indicates that the genus *glycosmis* is a potential bioactive natural product. Phytochemical investigations have shown that *glycosmis* plants produce diverse secondary metabolites and are a potential source of novel molecules. The structural diversity is the proof of multiple pharmacological effects. The review encourages further study of other species of the genus *Glycosmis* whose chemistry and biological activities still remain unexplored, with available information showing potential health applications and therapeutic uses of *Glycosmis* genus. Due to wide chemical diversity between medicinal plants of *Glycosmis* genus, it is necessary to develop a correlation between the chemical components and the pharmacologic/therapeutic action in future studies.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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