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Hypericum source of natural antimicrobials

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SUMMARY

Plants of the genus *Hypericum* (Family - Hypericaceae) are herbs, shrubs or small trees and are distributed chiefly in the temperate regions of the world. About 400 different species of *Hypericum* are available throughout the globe and 20 species occur in India, including a few cultivated in gardens. Almost all plants of the genus *Hypericum* are widely used in folk medicine. Several potent phytoconstituents from different *Hypericum* species have led to the isolation of antibacterial, antifungal and cytotoxic compounds. With the development of resistance and cross resistance with different microorganisms and the evolution of so many deadly diseases the screening and evaluation of the phytoconstituents so much so the development of varied phytoconstituents for the drug development for these deadly diseases is utmost essential in every aspects. The present review on the antimicrobial use of different *Hypericum* reports the findings from and extensive literature search on the *Hypericum* species around the globe that have been assessed for antimicrobial and antiviral activity. An attempt has been made through this review to summarize the information in this aspect in order to highlight the promising species of this genus which are worthy for further investigation as leads for drug development. Over 31 different Hypericum species have been reported to possess such activities with their varied number of phytoconstituents. Sixteen different constituents of six different classes of phytoconstituents have been reported to be present in different varieties of Hypericum, which may be considered responsible for this activity.

Key words: *Hypericum*; Antibacterial; Antifungal; Antiviral; Phytoconstituents

INTRODUCTION

Hypericum is a well known plant in herbal medicine for the therapeutic efficacy of its different species. The most potent species of this genus is *Hypericum perforatum* Linn. The genus Hypericum is well known for the therapeutic efficacy of its most potent species *Hypericum perforatum* Linn. Numerous compounds with documented biological activities have been reported from it (Upton, 1997).

About 400 species of *Hypericum* are spread world wide, and about 20 species are found in India (Hobbs, 1989; Anonymous, 1962). The genus *Hypericum* belongs to family Hypericaceae. These plants are mainly small shrubs or small trees (Anonymous, 1962). Height varies from 5 cm to 3 cm. All the species shows lots of morphological variation. There was disapproval of some botanists to place genus *Hypericum* in segregate family Hypericaceae, they believe it belongs to family Guttiferae, but morphological and phytochemical differences are not sufficient to separate these two families (Robson, 1997; Taskhtajan, 1980). Almost all plants of the genus *Hypericum* are widely used in folk medicine. Several phytochemical investigations on *Hypericum perforatum* have led to the isolation of antimicrobial (Rocha *et al.*, 1995), antifungal (Khosa *et al.*, 1982) and cytotoxic compounds (Weyerstahl *et al.*, 1995). Many therapeutic properties of different components of *Hypericum perforatum* have been reported in the American Herbal Pharmacopoeia (Upton *et al.*, 1997; Bombardelli, 1995). Extracts of

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Hypericum perforatum have been shown to be more effective than placebo in the treatment of depression (Linde *et al.*, 1996) and different phytochemical constituents of this plant like xanthones and flavonoid - hyperforin have been shown to be effective antimicrobials, antivirals and antibacterials against gram-positive bacteria, and to possess wound-healing potential (Bystrov, 1975; Gurevich *et al.*, 1971; Holzl *et al.*, 1989; Kitanov *et al.*, 1987; Lavie *et al.*, 1995; Bombardelli, 1995).

In India they are widely distributed in Assam, Jammu & Kashmir, Himachal Pradesh, Uttar Pradesh (Garhwal), Sikkim, West Bengal, Meghalaya, Arunachal Pradesh, Kerala and Tamilnadu (Anonymous, 1992; Asolkar *et al.*, 1992). Out of all the species available in India Nilgiri district of Tamilnadu play a major role in its content (Anonymous, 1962; Fyson, 1974). Three species are more prominent in this region viz. *Hypericum mysorense* Wight. and Arn. (commonly known as Shrubby St. John's Wort'), *Hypericum patulum* (commonly known as 'Tumbhul' - in Bihar; 'Uralo' in Nepal; La-san-rit - in Assam; 'Paharia'-in Bengal), *Hypericum hookerianum* (commonly known as Mehandi phul in Nepal) are abundantly available every where in the Nilgiris down, near to Kotagiri and Pykara (Fyson, 1974). All of these are erect, glabrous shrub, 1-3 m height with sessile leaves, horizontal with tips curved slightly upwards, narrow elliptic lanceolate with strong midribs (Fyson, 1974; Gamble, 1984; Rajan *et al.*, 2002). Almost all the folklore claims on these three species available at Nilgiris has been scientifically proved and their psychopharmacological (Mukherjee *et al.*, 2000a), wound healing (Mukherjee *et al.*, 2000b; 2000c; 2000d), antibacterial (2001, 2002) profiles have been reported.

Hypericum perforatum commonly known as St. John's wort is the most popular member of the *Hypericum* family and so many reviews on its different profiles have been reported (Bombardelli, 1995). This plant was used in ancient Greece, in folklore medicines. There are many ancient superstitions regarding these herbs. Their name Hypericum is derived from Greek and means Over an apparition; a reference to the belief that the herb was so obnoxious to evil spirits that a whiff of it would cause them to fly. (Grieve, 1994). The napthodianthrones, hypericine and pseudohypericin, different flavonoids like quercetin, hyperin etc., phluroglucinols, essential oils and xanthones has been reported to produce antidepressant, anti microbial, antioxidant, and antiinflammatory activity (Bystrov, 1975; Gurevich *et al.*, 1971; Holzl *et al.*, 1989; Kitanov *et al.*, 1987; Rocha *et al.*, 1995; Khosa *et al.*, 1982; Weyerstahl *et al.*, 1995). Different species of Hypericum possess antimicrobial and antiviral activities depending on their varied constituents. Based on these concepts a complete review on the various aspects of the antimicrobial usage of different species of this potent plant species has been made in this review.

ANTIBACTERIAL POTENTIALS OF *HYPERICUM*

Various Hypericum species with antibacterial activity

The plants of *Hypericum* genus are widely used for their various significant therapeutic activities. The available plethora of literature has proved the therapeutic efficacy of these plants for their antibacterial properties which has been explained further in Table 1.

The antimicrobial activity of the leaves and stems extract of two different varieties of *Hypericum* was evaluated by the disc diffusion method. Petroleum ether, acetone, chloroform and methanol extracts of the *Hypericum mysorense* and *Hypericum patulum* stems and leaves were investigated for their antimicrobial activity against six different strains of bacteria and fungi by zone of inhibition method (ZIM). The results showed that both the stem and leaf extracts of both species have a very broad spectrum of antibacterial activity. The petroleum ether and acetone extract of the leaves and stems of *H. mysorense* did not show antifungal effects against any of the six fungal organisms tested but other extracts showed a potential anti-fungal effect which was comparable to that of griseofulvin, the standard antifungal agent. Thus these results demonstrate that the leaf and stem extracts of both the *Hypericum* species has a very broad spectrum of activity and suggest that they may be useful in the treatment of various microbial infections (Mukherjee *et al.*, 2002a). *Hypericum hookerianum* is the common ornamental plant in the garden, when chloroform, acetone and methanolic

Table 1. Different Hypericum species with their antimicrobial potentials

Hypericum species	Solvent used for extract	Active against	Inactive against	References
H. androsaemum	Ethanol-Water	*SL/SA*	*EC*	Bhakuni *et al.* (1974)
H. avicularifolium	Acetone	*BS/EC/ST/SA*	*ML/CA/CU*	Sakara *et al.* (1990)
	MeOH	*BS*	*CA/CU/EC*	
	$CHCl_3$	*ST/SA/ML*	*EC/BS*	
H. brasiliense	Petrol	*BS*	-	Roch *et al.* (1995)
	$CHCl_3$	-	*BS*	
H. calycinum	Acetone	*BS/ML/ST/SA*	*EC/CA/CU*	Sakara *et al.* (1990)
	MeOH	*BS/ML/ST/SA*	*EC/CA/CU*	
	$CHCl_3$	*BS/ML/ST/SA/EC/CU*	*CA*	
H. chinense	MeOH	*BS*	*EC*	Nagai *et al.* (1987)
H. cordifolium	MeOH	*BS/SM/SA/SF/MG/TM/VS/HSV*	*EC/PA/ST/AF/PV*	Taylor *et al.* (1995) Taylor *et al.* (1996)
H. drummondii	Hexane	*BS/SA*	-	Jayasuriya *et al.* (1983)
H. elodeoides	MeOH	*BS/SM/SA/SF*	*EC/PA/HSV/PV/VS*	Taylor *et al.* (1995) Taylor *et al.* (1996)
H. typhimurium	MeOH	*MG/TM/AF*	*CA/SC*	Taylor *et al.* (1995)
H. empetrifolium	H_2O	*BP-PHI, T7, T2, T4, M52*	-	Delitheos *et al.* (1992)
H. erectum	MeOH	*SA*	-	Kitagaw *et al.* (1987)
H. ericoides	MeOH	*SA*	*EC/KP/PA*	Rios *et al.* (1987)
	$CHCl_3$	*SA/CA*	*EC/KP/PA*	
H. galioides	H_2O	*SA/EC/TM/CA/SC*	*BS/PA/AN*	Mechesney *et al.* (1985)
	Cyclohexane	*SA/TM/AN/CA/SC*	*EC/BS/PA*	
	Ethyl acetate	*BS/SA/CA/SC*	*EC/PA/TM/AN*	
H. gentianoides	H_2O	*BS/SA/EC/TM/CA*	*PA/AN/SC*	McChesney *et al.* (1985)
	Cyclohexane	*PA/BS/SA/SC*	*EC/AN/TM/CA*	
	Ethyl acetate	*PA/BS/SA/EC/TM/SC/CA*	*AN*	
H. hircinum	H_2O	*SMU/SS/SA/SO/EC/PVU*	*PA*	Barbagallo *et al.* (1987)
	MeOH	*SMU/SS/SA/SO/EC*	*PVU/PA*	
	$CHCl_3$	*PA/SMU/SS/SA/SO*	*EC/PVU*	
	Pet. ether	*SMU/SS/SA/SO/EC/PVU*	*PA*	
H. Hookerianum	$CHCl_3$	*PC/BM/BC/BS/SA/EC*	-	Mukherjee *et al.* (2001)
	Acetone	*PC/BM/BC/BS/SA/EC*	-	
	MeOH	*PC/BM/BC/BS/SA/EC*	-	
H. japonicum	ETOH	*HBV/HSV*	-	Minshi (1989)
H. lanuginosum	Acetone	*BS/SA/SSO*	-	Sakar *et al.* (1988)
	ETOH	*BS/SA/SSO*	-	
	$CHCl_3$	*SA/SSO*	*BS*	
	Ethyl acetate	*CU*	-	
H. maculatum	H_2O	*CK/CT*	*AFL/AF/CA/CP*	Chaumont *et al.* (1978)
H. montbretii	Acetone	*SA*	*BS/EC/ML/ST/CA*	Sakara *et al.* (1990)
	MeOH	*SA*	*BS/EC/ML/CU/ML*	
	$CHCl_3$	*BS/EC/ST/SA/CA/CU*	-	
H. mysorense	Pet ether	*PC/BM/BC/BS/SA/EC*	*CA/CT/CN*	Mukherjee *et al.* (2002)
	$CHCl_3$	*PC/BM/BC/BS/SA/EC/CA/CT/CN*	-	
	Acetone	*PC/BM/BC/BS/SA/EC*	*CA/CT/CN*	
	MeOH	*PC/BM/BC/BS/SA/EC/CA/CT/CN*	-	
H. origanifolium	Acetone	*BS/SA/SSO/CU*	-	Sakara *et al.* (1988)
	$CHCl_3$	*BS/SA/SSO/EC/ST*	-	
	Ethanol	*BS/SSO/CU*	-	
	Ethyl acetate	*SA/SSO/PA*	-	
H. patulum	MeOH	-	*BS/EC*	Ishii *et al.* (1984)
H. patulum	Pet ether	*PC/BM/BC/BS/SA/EC/CA/ CT/CN*	-	Mukherjee *et al.* (2002)
	$CHCl_3$	*PC/BM/BC/BS/SA/EC/CA/CT/CN*	-	
	Acetone	*PC/BM/BC/BS/SA/EC/CA/CT/CN*	-	
	MeOH	*PC/BM/BC/BS/SA/EC/CA/CT/CN*	-	

Table 1. Different Hypericum species with their antimicrobial potentials

Hypericum species	Solvent used for extract	Active against	Inactive against	References
H. perfoliatum	H_2O	*SA/SO*	*EC/PVU/PA/SMU*	Barbagallo *et al.* (1987)
	Pet ether	*SA/SO/PVU/PA/EC/SS*	-	
	$CHCl_3$	*SA/SO*	*EC/PVU/PA/SS*	
	MeOH	*SO*	*EC/PVU/PA/SS/SA/SMU*	
H. perforatum	Acetone	*IV*	-	Mishenkova *et al.* (1975);
	MeOH	*PVU/BS/MC/SMU/MG/SA*	*KP/SM/AFL/AF/ TM/CA/SC/PA*	Grauds (1997); Mccutchon *et al.* (1992).
	H_2O	*IV/HSV/VV/SO*	*PV/EC/PVU/PA/SA/SMU*	
	$CHCl_3$	*SA/SO*	*EC/PVU/PA/SS*	
	Ethyl acetate	*IV*	-	
	Pet. ether	*PVU/PA/SA/SMU/SO/SS*	-	
	ETOH	*ST*	-	
H. reflexum	MeOH	*SA/BS/ML/KP*	*PA/EC*	Herrera *et al.* (1996)
	$CHCl_3$	*SA/ML*	*EC/PA*	
H. salsugineum	$CHCl_3$	*EC/PA/SA/SSO/BS/ST/CU*	-	Sakara *et al.* (1988)
	ETOH	*EC/SSO/BS/ST/CU/SA*	-	
	Ethyl acetate	*SA/SSO*	-	
H. scabrum	ETOH	*SA*	*CA*	Alshamma *et al.* (1979)
H. triquetrifolium	MeOH	*BS/ST/SA/EC*	*ML/CA/CU*	Sakara *et al.* (1990)
	Acetone	*BS/ST/SA*	*EC/ML/CA/CU*	
	$CHCL_3$	*BS/ST/SA/ML/CA/CU*	*EC*	
H. uliginosum	ETOH-H_2O	*SA/TM*	-	Taylor *et al.* (1969)

FL=Aspergillus flavus; *AN=Aspergillus niger*
AF=Aspergillus fumigatus; *BS=Bacillus subtilis*
BM=Bacillus megaterium *BC=Bacillus coagulans*
CA=Candida albicans; *CN=Cryptococcus neoformans*
CP=Candida parapsilosis; *CU=Candida utilis*
CK=Candida krusei; *CT=Candida tropicalis*
EC=Escherichia coli; *HBV=Hepatitis B virus;*
IV=Influenza virus; *MC=Microsporum cookei*
KP=Klebsiella pneomoniae;
MG=Microsporum gypseum; *TM=Trichophyton mentagrophytes*
PA=Pseudomonas aeruginasa;
PC=Pseudomonus cepacia *SSO=Streptococcus sorbinus*
PV=Polio virus; *SC=Saccharomyces cerevisiae*
SL=Sarcina lutea; *SA= Staphylococcus aureus*
SM=Serratia marcescens; *SF=Streptococcus faccalis*
SMU=Streptococcus mutans; *SS=Streptococcus sanguis*
SO=Staphylococcus oxford; *PVU=Proteus vulgaris*
ST=Salmonell typhimurium; *ML=Micrococcus luteus*
VS=Virus sindbis; *HSV=Herpes simplex virus*
VV=Vaccinia virus; *- = No activity reported*

extracts of leaves and stem were investigated against six different gram +ve and gram -ve bacteria. The stem showed maximum antibacterial activity (Mukherjee *et al.*, 2001a). The methanolic extracts of *H. hookerianum* (Mukherjee *et al.*, 2000b), *H. mysorens* (Mukherjee *et al.*, 2000c) and *H. patulum* (Mukherjee *et al.*, 2000d) have been found to possess significant wound healing activity (Mukherjee, 2002b).

The ethanolwater extract of *Hypericum androsaemum* when tested against three different bacteria it was found to have activity against *Sarcina lutea* and *S. aureus*, while inactive against *E. coli* (Bhakuni *et al.*, 1974). This plant also reported to have wound healing activity (Vickery, 1981). Acetone, Chloroform and Methanol extract of dried flowers and leaves of *Hypericum avicularifolium* has been reported to have activity against various bacteria like *Bacillus subtilis, Salmonella typhimurium, S. aureus* etc. while only acetone extract was active against *E coli.* When acetone, chloroform and methanolic extracts of *Hypericum calycinum* were tested against same bacteria they were found to have activity against many of them. But only chloroform extract was found to be active against *E. coli* (Sakara *et al.*, 1990).

Nagai *et al.* (1987) reported the activity of methanolic extract of *Hypericum chinese* flowers against *B. subtilis*, while it was found inactive against *E. coli*. The methanolic extract of fresh leaves of *Hypericum cordifolium* and methanolic extract of fresh root of *Hypericum elodeoides* were studied by Taylor *et al.* (1995a) and was reported to have activity against *B. subtilis, Serratia marcescens, S. aureus,* and *Streptococcus faecalis* while inactive against *E. coli, Pseudomonous aeruginosa* and *Salmonella typhimurium*. The hexane extract of dried leaf and dried root of *Hypericum drummondii* were found to be active against *Bacillus subtilis* and *S. aureus* (Jayasuria *et al.*, 1989). The methanolic extract of dried aerial parts of *Hypericum erectum* was reported to be active against *S. aureus* (Kitagawa *et al.*, 1987).

The methanolic and chloroform extracts of aerial parts of *Hypericum ericoides* when investigated for antibacterial activity, both extracts showed weak activity against *S. aureus*, while both of them was found to be inactive against *E. coli, Klebsiella pneomonia* and *Pseudomonas aeruginosa* (Rios *et al.*, 1987).

The cyclohexane, ethyl acetate and water extracts of dried aerial parts of *Hypericum galioides* and *Hypericum gentianoides* have been reported to have activity against various bacteria (Mc Chesney *et al.*, 1985). It was found that the activity of the extracts was mainly dependent upon solvent used for the extraction. In case of *Hypericum glioides* cyclohexane and ethyl acetate extracts were inactive against *E. coli* but aqueous extract showed activity.

Chloroform, methanol, petroleum ether and aqueous extracts of dried arial parts of *Hypericum hircinum* has been evaluated for their antibacterial potentials and most of these extracts showed activity against *Streptococcus mutants, S. sanguis, S. aureus, S. oxford* and *E. coli*. When same solvent extracts of dried aerial parts of *Hypericum perforatum* were evaluated, only petroleum ether extract showed activity against maximum number of strains of bacteria (Barbagallo *et al.*, 1987). *Hypericum lanuginosum, Hypericum origanifolium and Hypericum salsugineum* showed activity against *S. aureus, S. sorbinus and B. subtilis,* when extracted with acetone, chloroform, ethyl acetate and ethanol (Sakara *et al.*, 1988). *Hypericum montbret* and *Hypericum triquetrifolium* showed antibacterial activity against *S. aureus, B. subtilis, E. Coli* and *S. typhimurium* when dried leaves and flowers were extracted with chloroform, acetone and methanolic extracts of some plant showed activity against only *S. aureus* (Sakara *et al.*, 1990). Though the methanolic extract of *Hypericum patulum* is inactive against *B. subtilis* and *E. coli*, (Ishii *et al.*, 1984), it showed wound healing activity in excision and incision models in rat (Mukherjee *et al.*, 2000d).

Methanolic and chloroform extracts of entire plant *Hypericum reflexum* showed activity against *S. aureus, S. epidermidis, B. cereus , B. subtilis* and *Micrococcus luteus* (Herrera *et al.*, 1996). Ethanol extract of dried aerial parts of *Hypericum scabrum* showed antibacterial activity against *S. aureus* (Al-shamma *et al.*, 1979). *Hypericum uliginosum* showed antibacterial activity against *S. aureus*, when extracted with ethanol water (Taylor *et al.*, 1969).

Hypericum perforatum is the most popular species of the genus beside its significant antidepressant and other pharmacological actions, its antimicrobial activities are also reported. Its various extracts showed antibacterial action against different strains of microorganisms, these activities are summarized in Table 1.

Different phytoconstituents of Hypericum species with antibacterial potential

Numerous compounds with documented biological activities has been reported from *H. perforatum* e.g. napthodianthrones, hypericin and pseudohypericin, different flavonoids like quercetin, hyperin etc., phloroglucinols, essential oils and xanthones has been reported to produce antidepressant, anti microbial, antioxidant, and antiinflammatory activity (Upton, 1997; Bystrov, 1975; Gurevich *et al.*, 1971; Holzl *et al.*, 1989; Kitanov *et al.*, 1987; Rocha *et al.*, 1995; Khosa *et al.*, 1982; Weyerstahl *et al.*, 1995). The different extracts as well as the different phytochemical constituents of this plant like xanthones and the flavonoid - hyperforin have been shown to be effective as antiviral and antibacterial against gram positive bacteria and possess wound healing potentials (Lavie *et al.*, 1995; Bombardelli, 1995).

Thus various species of *Hypericum* have been reported to possess antibacterial activity and many of them were reported to have potentials antibacterial activities comparatively at lower concentrations.

Table 2. Phytoconstituents responsible for antimicrobial and antiviral activity from various species of *Hypericum*

Constituents	Activity	Plants	Reference
Phloroglucinol	Antibacterial	*H. perforatum*	Bystrov 1975; Gurvich *et al.*, 1971
		H. japonicum	Yamaki *et al.*, 1994; Ishiguro *et al.*, 994
		H. brasiliense	Rocha *et al.*, 1995, 1996
		H. hirsutum	Umek *et al.*, 1990
		H. macultum	
		H. tetraptetum	
		H. montanum	
		H. humifusum	
Xanthones	Antibacterial, antifungal and Antiviral	*H. perforatum*	Upton, 1997
		H. brasiliense	Rocha *et al.*, 1994
		H. paturum	Ishiguro *et al.*, 1993
		H. patulum	Ishiguro *et al.*, 1995a,b
		H. androsaemum	Niesen *et al.*, 1979
Hpericine	Antiviral	*H. perforatum*	Lavie *et al*, 1995; Meruelo *et al.*, 1988
		H. hirsutum	Umek *et al.*, 1994; Karting *et al.*, 1996; Brantner *et al.*, 1994
		H. maculatum	
		H. tetrapterum	
		H. montanum	
		H. humifusum	
		H. tomentosum	
		H.bithynicum	
		H. glandulosum	
		H. balearicum	
Pseudo hypericin	Antiviral	*H. perforatum*	Meruelo *et al.*, 1988
		H. hirsutum	Umek *et al.*, 1994; Karting *et al.*, 1996; Brantner *et al.*, 1994
		H. maculatum	
		H. tetrapterum	
		H. montanum	
		H. humifusum	
		H. tomentosum	
		H.bithynicum	
		H. glandulosum	
		H. balearicum	
Proanthrocyanidin	Antibnacterial, antifungal and antiviral	*H. perforatum*	Upton 1997
Essential oils	Antifungal	*H. perforatum*	Khosa *et al.*, 1982

Various phytoconstituents of *H. perforatum* responsible for antimicrobial potentials has been shown in Table 2 and few phytoconstituents has been shown in Fig. 1. Hyperforin (I) a phloroglucinol derivative has potent antibacterial activity against gram positive bacteria and also reported to have wound healing activity (Bystrov, 1975; Gurevich *et al.*, 1971). Xanthones are also reported to have antimicrobial activity. Yamaichi *et al.* (1994) reported the antimicrobial activity of Phloroglucinol isolated from *Hypericum japonica*, against *Staphylococcus aureus*. Ishiguro *et al.* (1987) reported saroapidin A, B, and C, (II) isolated from *Hypericum japonicum* as antibiotic compounds, same author in 1990 reported the antimicrobial activity of sarothrali G, isolated from *Hypericum japonicum*.

Ishiguro and co-workers (1994) isolated two new phloroglucinol derivatives viz. sarothralen C and D (III) from the methanolic and ether extract of whole plant of *Hypericum japonicum*, which has

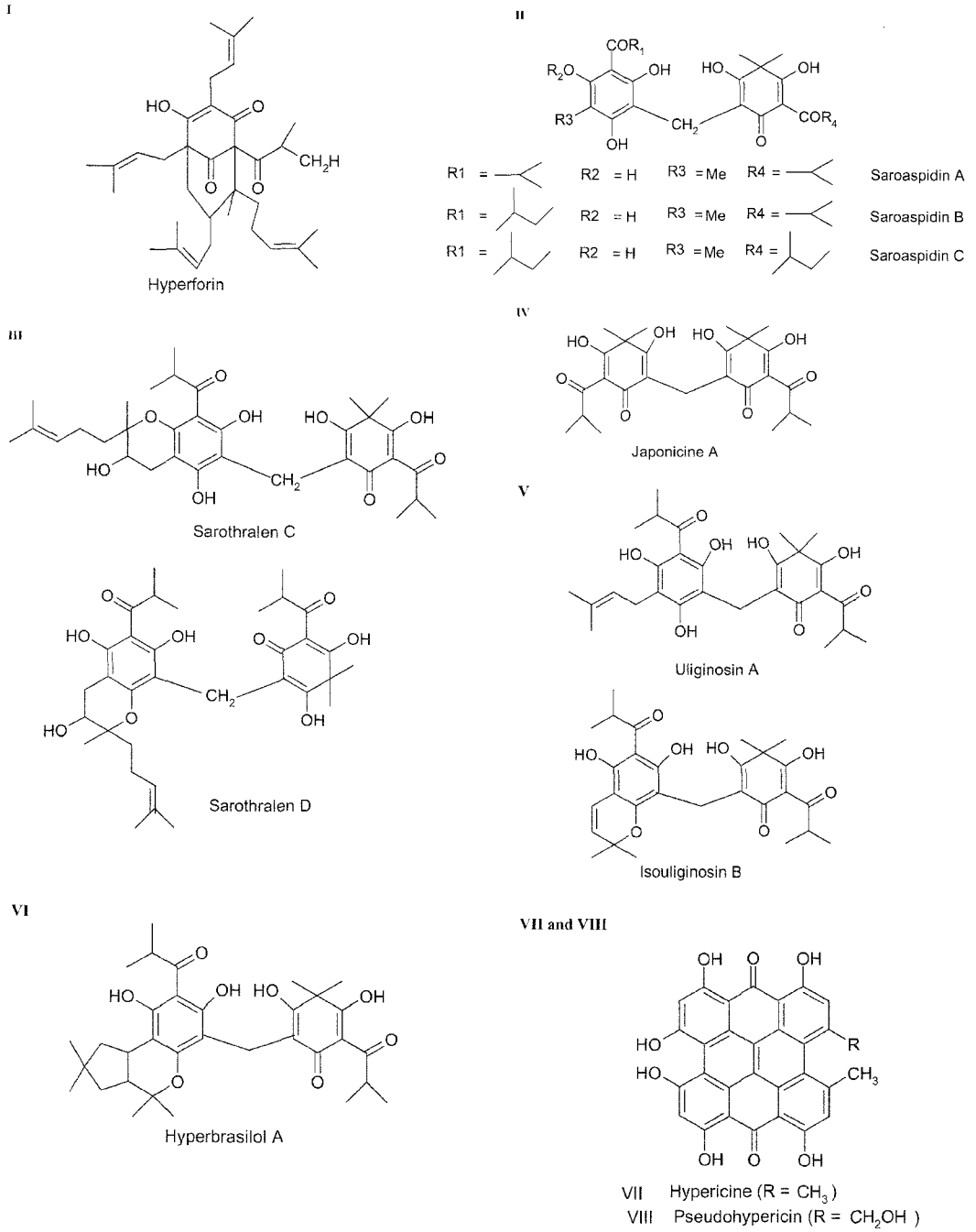

Fig. 1. Phytoconstituents of *Hypericum* Species with antimicrobial potentials.

been reported to have antibacterial activity against *S. aureus.* Four phloroglucinol derivatives viz. Japonicine-A (IV), uliginosin-A, isouliginosin-B (V) and hyperbrasilol-A, isolated from *Hypericum brasiliense* petrol extract are reported to have activity against *Bacillus subtilis.* New phloroglucinol viz. hyperbrasilol B has been reported from the petrol extract of leaves and flowers of *Hypericum brasiliense,* and three new phloroglucinol were found to have antibacterial activity against *B. subtilis* (Rocha *et al.*, 1995; 1996).

The xanthones compounds are responsible for the antimicrobial activities of *Hypericum perforatum* (Upton, 1997). The literature survey shows the presence of xanthones in many other species of *Hypericum* viz. *Hypericum paturum* (Ishiguro *et al.*,

1993), *Hypericum patulam* (Ishiguro *et al.*, 1995a; 1995b), *Hypericum androsaemum* (Nielsen *et al.*, 1979). Hyperforin which is a well proved antibacterial phytoconstituents was also found to be present in many *Hypericum* species like *Hypericum perforatum, Hypericum hirsutum, Hypericum maculatum, Hypericum tetraptetum, Hypericum montanum, and Hypericum humifusum* (Umek *et al.*, 1990) which are responsible for the antibacterial activity of other *Hypericum* species except *H. perforatum*.

ANTIFUNGAL POTENTIALS OF *HYPERICUM*

Different *Hypericum* species with antifungal activity

Various plant extracts of *Hypericum* has been reported to have antifungal potentials. The potential species for this purpose has been explained in Table 1. The acetone, chloroform and methanol extracts of dried flowers and leaves of *Hypericum avicularifolium, Hypericum calycinum, Hypericum montbretii* and *Hypericum triquetrifolium* when investigated for anti-yeast activity, only chloroform extracts were found to be active against *candida utilis* (Sakara *et al.*, 1990). Methanolic extract of fresh leaves of *H. cordifolium* showed antifungal activity against *Microsporum gypseum* and *Trichophyton mentagrophytes*. The activity was enhanced with exposure to UV light (Taylor *et al.*, 1995a). *Hypericum gentianoides* and *Hypericum galioides* showed antifungal activity against various fungi strains, when extracted with cyclohexane and ethyl acetate (Mc Chesney *et al.*, 1985). Aqueous extract of dried aerial parts of *Hypericum hirsutum* was proved active against *Candida krusei, Candida parapsilosisi, C. pseudotropicalis* and *C. tropicalis*, while aqueous extract of *H. maculatum* has activity against *C. Krusei* and *C. tropicalis* (Chaumont *et al.*, 1978a).

Antiyeast activity of *H. lanuginasum, H. origanifolium* and *H. salsugineum* has been reported by Sakara *et al.* (1988). Aqueous extract of fresh entire plant of *H. pilchard* is reported to have antifungal activity against pathogenic fungi *Pestaalotia funerea, Aclerotinia trifoliorum* and *Stereum purpureum* (Chaumont *et al.*, 1978b). *Hypericum revolutum* is reported as active against various fungi (Decosterd *et al.*, 1987).

Methanolic extract of *Hypericum perforatum* has been reported to possess weak activity against *Microsparum cookei* and *Microsporum gypsum* but ethanol extract has been reported activity against various other fungi. (Mc Cutecheon *et al.*, 1994; Khosa *et al.*, 1982).

Different phytoconstituents of *Hypericum* species with antifungal potential

The antifungal activities of *Hypericum perforatum* are supposed to be due to the essential oil. The essential oil of this plant contain monoterpenes and sesquiterpene (caryaphyllen, humulene) (Khosa *et al.*, 1982; Sticher, 1977; Chialva, 1981; Mathis, *et al.*, 1964). The oil is also said to have the use as sunscreen, which is disputed. The oil has been used in commercial sunscreen products. But reports of its efficacy are contradictory (Proserpio, 1976; Anonymous, 1992). Hyperbrasilone (VI) which is γ-pyrone and various xanthones isolated from the *Hypericum brasiliense* has been shown anti-fungal activity aganist *Cladosporium cucumerrinum* (Rocha *et al.*, 1994). The antifungal properties of different phytoconstituents of Hypericum have been explained in Table 2 and few phytoconstituents has been shown in Fig. 1. The various xanthone derivatives have been also reported to have antifungal potentials (Upton, 1997). More investigations are required to find out the antifungal activity of various phytoconstituents occurs in different species of this genus, against various pathogenic fungi.

ANTI VIRAL SPECTRUM OF DIFFERENT SPECIES OF *HYPERICUM*

Different *Hypericum* species with antiviral potential

St. John's Wort' or *H. perforatum* is the popular member of genus *Hypericum* which is being used from the time of the ancient Greeks for its varieties of Pharmacological and antimicrobial activities. Many writers like Hippocrates, Pliny, Dioscorides, Theophrastus and Galen has mentioned about its medicinal properties (Upton, 1997). It is very popular as a antidepressant in America and European countries. This plant has got more importance due to the presence of hypericin, which is said to have antiviral activity against HIV infestation.

Hypericum perforatum showed antiviral activity against *Influenza virus* (Mishenkova, 1975), *Herpes*

simplex virus type 2 and *Vaccinia virus* (May *et al.*, 1978). When hypericin isolated from *H. perforatum* was investigated as a chemotherapeutic agent for HIV inflection, it was found effective in inhibition of replication cycle of virus. (Vilietinck *et al.*, 1998). When 18 patients with acquired immunodeficiency syndrome (AIDS) were treated with intra-venous *Hypericum* preparation and tablets of different dosage 16 patients out of 18 responded the treatment and 14 patients out of those 16 remained clinically stable (Steinbeck *et al.*, 1993). Though hypericin has given the hope for treatment of HIV infection, the proper concentration required for efficacy is not known. In large dosage it may cause photosensitization as has been reported in case of various animals, which are either grazing on *Hypericum* or given the dosage of hypericin (Munscher, 1961; Southwell *et al.*, 1991; Horsley, 1934).

From past many years the antiviral activities of various species of this genus has been investigated and many of them are proved to have antiviral activities. The dried roots juice *H. cardifolium* and *H. uralum* has shown activity against *Polio virus -1, Herpes simplex-1 and Sindbis virus* (Taylor *et al.*, 1996). Aqueous and ethanol extracts of *Hypericum japonicum* showed strong activity against *Hepatitis B virus* and *Herpes simplex* 2 virus (Minshi 1989, Zheng *et al.*, 1992).

Different phytoconstituents of *Hypericum* species with antiviral potential

Many authors have reported the antiviral activities of hypericin (VII) and pseudohypericin (VIII), which are the phytoconstituents present in the *H. perforatum* and many other species of *Hypericum* (Meruelo *et al.*, 1988; Weber *et al.*, 1994; LopezBazzocchi *et al.*, 1991; Wood *et al.*, 1990). Xanthones present in the *Hypericum perforatum* also have antiviral potentials (Upton, 1997; Hobbs, 1989) various other xanthones are present in many other species of *Hypericum*, so it is needed to investigate their possible antiviral potentials of those phytoconstituents like xanthones, hypericin and pseudohypericin etc. which are reported to be present in many other varieties viz. *H. hirsutum, H. maculatum, H. tetrapterum, H. montanum, H. humifusum, H. tomentosum, H. bithynicum, H. glanddulosum* and *H. balearicum* (Umek *et al.*, 1994). The antiviral potentials of various *Hypericum* species may be due to presence of hypericin, pseudohypericin and xanthones, to find out the possible anti-viral potentials of various species of *Hypericum*, more phytochemical investigations and antiviral activity studies are required. The antiviral potentials of various phytoconstituents of different *Hypericum* species have been shown in Table 2 and few phytoconstituents has been shown in Fig. 1.

CONCLUSIONS

The resurgence of the microbial and viral diseases has been known to occur in its various resistant from time to time in endemic and epidemic proportions all over the world. From time immemorial the cure of these diseases has been attempt by the traditional medicine. Scientific validation and screening for new phytotherapeutic agents from this traditional knowledge has helped for the drug development with the emergence of resistance and cross resistance to some standard drugs used in these particular infections. Over 31 different *Hypericum* species and various compounds derived from them have been evaluated for their antibacterial, antifungal and anti viral potentials. Composite or non-specific activities of plant extracts are apparently significant in the uses and cure with traditional knowledge. The data complied in Table 1 reveal that extracts of different *Hypericum* species from the same family have shown varied anti microbial and antiviral potentials. Table 2 showed the potent plant derived phytoconstituents from this particular species responsible for these activities. This review on the combined approaches of exploration and exploitation of the different species of Hypericum for their uses in the field of bacterial and viral infection will definitely throw further light to different findings for the exploitation of the lead compounds for treating the deadly ailments and in one hand and to restore confidence in the use of *Hypericum* in the other.

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