



Review Article

A REVIEW ON PLANTS OF GENUS *POLYGONATUM*.

Sandeep K. Singh¹, Seema Singh^{2*}, Sanjeev K Verma³, Piyush Jain¹, Vinod K. Dixit¹, Sanjeev Solanki¹.

1. Department of Pharmaceutical Sciences, Dr. H.S.Gour University, Sagar-470001. India.
2. Northern India Engineering College, Department of Pharmacy, Lucknow U.P. India
3. King George Medical University, Department of Pulmonary Medicine, Lucknow U.P.

*Corresponding Author: Email seemapharma1987@gmail.com

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ABSTRACT

Plants of genus *Polygonatum* (Ruscaceae) are widely used in traditional medicine to cure many diseases such as ageing, antioxidative action, insecticidal, antiherpetic, antinociception and aphrodisiac. A variety of phytoconstituents has been isolated from the *Polygonatum* species which include lignans, flavonoids, coumarins, steroids, terpenes, fatty acids and aliphatic long chain compounds. Anti-inflammatory, analgesic, antidiarrhoeal, antimicrobial, antioxidant, antimalarial and insecticidal activities have been reported in the extracts of these plants and their phytoconstituents. An overview of the ethnobotanical, phytochemical and pharmacological investigations on the *Polygonatum* species is presented in this review.

Keywords: *Polygonatum*, saponins, homoisoflavone, antinociceptive, Solomon's-seal.

INTRODUCTION

Since the beginning of human civilization, medicinal plants have been used by mankind for its therapeutic value. The use of traditional medicines and medicinal plants in most developing countries as therapeutic agents for the maintenance of good health. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. Herbs, spices, condiments, phytochemicals and medicinal plants are often used for the treatment and prevention of many human maladies (Heber, 2004).

This fast growing herbal sector has its roots in the very rich and diverse health care traditions of our country that include the codified systems like Ayurveda, Siddha, Unani, Tibetan

and Homeopathy on one hand and the largely oral folk traditions on the other. These traditions, having evolved in the lap of Nature, rely mainly on natural resources available in the surroundings with plants forming the major resource. In Indian traditions, all the plants are considered to have medicinal properties.

Polygonatum (King Solomon's-seal, Solomon's seal) is a genus of about 57 species belongs to family Liliaceae or Convallariaceae. It is widely distributed in East Asia, mainly China and Japan where 40 species of *Polygonatum* are found (Tamura, 1993). Solomon's seal has been used for thousands of years in herbal medicine. The rhizomes are adaptogenic, antioxidant, cardiogenic, demulcent, diuretic, energizer,

hypoglycemic and tonics are used in the treatment of dry coughs and pulmonary problems, including tuberculosis (Jiang, 1977, 1986). The antibacterial and antifungal activity of the *Polygonatum* has been reported (Alluri et al., 2006). *Polygonatum* reduced blood sugar level by different mechanisms including α -glucosidase inhibition and increased insulin sensitivity.

Traditional uses of selected species of *Polygonatum*

The plants of genus *Polygonatum* have been used by the tribal in various parts of Asia and Africa. Widely employed different species, their parts and mode of application/administration in various diseases are presented in Table 1.

Key classes of compounds common in *Polygonatum*:

The investigation for the phytochemistry of genus *Polygonatum* possibly began with worked on *Polygonatum sewerzowii* Regel. So far, a variety of interesting but limited compounds have been isolated/identified from the plants of this genus which include phenolics, steroids, triterpenes, tannins and alkaloids.

Phenolic compounds

Plant phenolics are a structurally diverse set of compounds responsible for organoleptic properties of plants. These are found to possess a wide range of therapeutic activity. They occur in plants in the form of simple phenolic acids or as complex structures associated with the oxygenated heterocyclic ring, such as benzoic acid derivatives, stilbenes, tannins, lignans, anthocyanins, flavonoids and coumarins (Harborne et al., 1999).

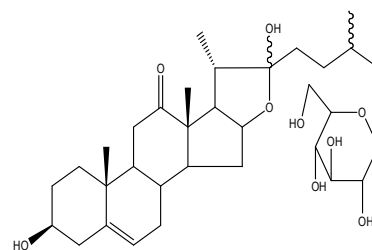
Lignans, another important class of plant phenolics, are formed as a result of dimerization of phenylpropanoid units at the central carbons of their side chains and generally occur in the root, stem, bark, fruit and seed parts of the plant.

Flavonoids, another important class of phenolics featuring the linkage of two benzene rings by a chain of 3 carbon atoms, so as to form pyran or pyrone ring, play predominant role in plant physiology and serve as light screens, antioxidants, enzyme inhibitors, precursors of toxic substances and pigments (Harborne et al., 1975; McClure, 1986).

Coumarins, another class of plant phenolics, comprised of phenyl propanoid system, are found to be physiologically effective for animals as well as men.

Steroids

Sterols, structurally comprised of per hydro cyclo penta- (O) phenantherene ring system, are widely distributed in higher plants (Harborne et al., 1999).



22-hydroxy-25 (R and S)-furost-5-en-12-on-3a, 22, 26-triol 26-O- β -D-glucopyranoside.

The steroids are modified triterpenoids containing the tetracyclic ring system of lanosterol, but lacking the three methyl groups at C-4 and C-14. Cholesterol typifies the fundamental structure, but further modifications, especially to the side-chain, help to create a wide range of biologically important natural products, e.g. sterols, steroidal saponins, cardioactive glycosides, bile acids, corticosteroids, and mammalian sex hormones. Because of the profound biological activities encountered, many natural steroids together with a considerable number of synthetic and semi-synthetic steroidal compounds are routinely employed in medicine (Paul M D, 2002).

Alkaloids

Alkaloids are naturally occurring plant compounds having a basic character and containing at least one nitrogen in a heterocyclic ring. These are 'physiologically active basic compounds of plant origin, in which at least one nitrogen atom forms part of a cyclic system. Interestingly, alkaloids represent one of the most important groups of chemical constituents occurring in the entire plant kingdom which exert extremely potent and vital physiological and pharmacological activities in the human beings. Therefore, it will be worthwhile to study the alkaloids with regard to the various aspects of alkaloids shall now be discussed adequately in a sequential manner so as to have a better in-depth of knowledge.

Furthermore, almost 15% of all vascular plants contain alkaloids. Alkaloids may occur in various parts of the plant. It may, however, be pointed out that in a particular species, normally only one or two specific organs and not all

organs, essentially afford the function of alkaloidal formation (Ashutosh Kar, 2007).

Terpenes

Terpenes constitute one of the largest and structurally diverse class of plant secondary metabolites responsible for flavor, fragrance and bioactivity of the plants.

In general, terpenoids may be defined as natural products whose structures are considered to be divided into several

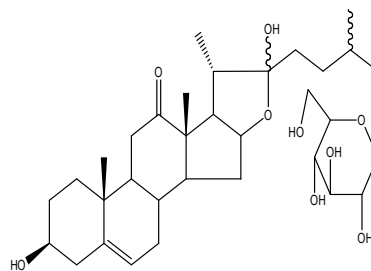
isoprene units; therefore, these compounds are invariably termed as isoprenoids. Besides, this particular group of compounds is sometimes collectively referred to as the terpenes in relatively older texts. Logically, the -oid suffix seems to be more acceptable and convincing, as it is in the same vein for steroids, alkaloids, flavonoids, etc. (Ashutosh Kar, 2007).

Table 1. Traditional uses of *Polygonatum* species.

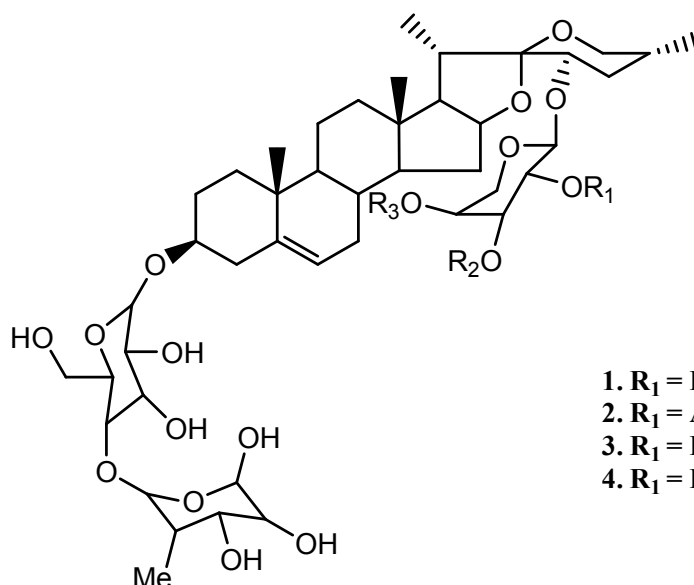
Species	Part	Mode	Indications	Country	References
<i>P. multiflorum</i>	Roots	Intraperitoneal injection	Ameliorating, cholinergic, serotonergic	Taiwan	Liu et al., 2007
<i>P. verticillatum</i>	Rhizomes	Suspension	Antimicrobial	Pakistan	Khan H. et al., 2012
<i>P. cyrtoneuma</i>	Rhizomes	Cell line study	Anti-tumor	China	Zhang Z. et al., 1983
<i>P. cyrtoneuma</i>	Rhizomes	Inhibition assays	Antiherpetic	China	Liu X., 2011
<i>P. cyrtoneuma</i>	Rhizomes	--	Antiherpetic, antiviral	China	Liu X. et al., 2011
<i>P. cyrtoneuma</i>	Rhizomes	--	Antineoplastic	China	Wang S. et al., 2011
<i>P. odoratum</i>	Rhizomes	Decoctions	Antityrosinase	China	Yan Y. et al., 2010
<i>P. odoratum</i>	Rhizomes	Expectorants	Respiratory diseases	Korea	Choong J. L. et al., 2006
<i>P. odoratum</i>	Rhizomes	Intraperitoneal injection	Anti-diabetic	China	Choi S B et al., 2002
<i>P. odoratum</i>	Rhizomes	--	Stomachs, diabetes	China	Qian Y. et al., 2010
<i>P. odoratum</i>	Rhizomes	Tissue culture	Apoptosis	China	Yang Y. et al., 2011
<i>P. sibiricum</i>	Roots	--	Respiratory diseases, Anti-diabetic	China	Choong J. L. et al., 2006
<i>P. sibiricum</i>	Rhizomes	--	Vital energy	China	Xia S. et al., 2006
<i>P. sibiricum</i>	Rhizomes	Intraperitoneal injection	Osteoporosis	China	Zeng G.F. et al., 2011
<i>P. sibiricum</i>	Rhizomes	--	Chemistry	Korea	Ahn M.J. et al., 2006
<i>P. punctatum</i>	Rhizomes	Cell line study	Cytotoxic	China	Yang Q.X. et al., 2006
<i>P. kingianum</i>	Rhizomes	--	Chemistry	Beijing	Yu H. et al., 2009
<i>P. kingianum</i>	Rhizomes	Incubation	Antimicrobial	China	Wang Y.F. et al., 2003
<i>P. verticillatum</i>	Rhizomes	In-vitro phytotoxicity assay	Phytotoxic, insecticidal and leishmanicidal	Pakistan	Saeed M. et al., 2010a
<i>P. verticillatum</i>	Rhizome	Intraperitoneal injection	Antinociceptive	Pakistan	Khan H. et al., 2010
<i>P. verticillatum</i>	Rhizomes	--	Antimalarial and free radical scavenging activity	Pakistan	Khan H. et al., 2011
<i>P. zanlanscianense</i>	Roots	Cell line study	Study the cytotoxicity	China	Ying W. et al., 2006

Glycoside

Glycosides, in general, are defined as the condensation products of sugars with a host of different varieties of organic hydroxy (occasionally thiol) compounds (invariably monohydrate in character), in such a manner that the hemiacetal entity of the carbohydrate must essentially take part in the condensation. It is, however, pertinent to state here that the polysaccharides are also encompassed in this broad-based overall definition of glycosides. The non-carbohydrate moiety is usually termed as aglycone (or aglycon), or a genin.



22-hydroxy-25 (R and S)-furost-5-en-12-on-3a, 22, 26-triol 26-O-β-D-glucopyranoside.



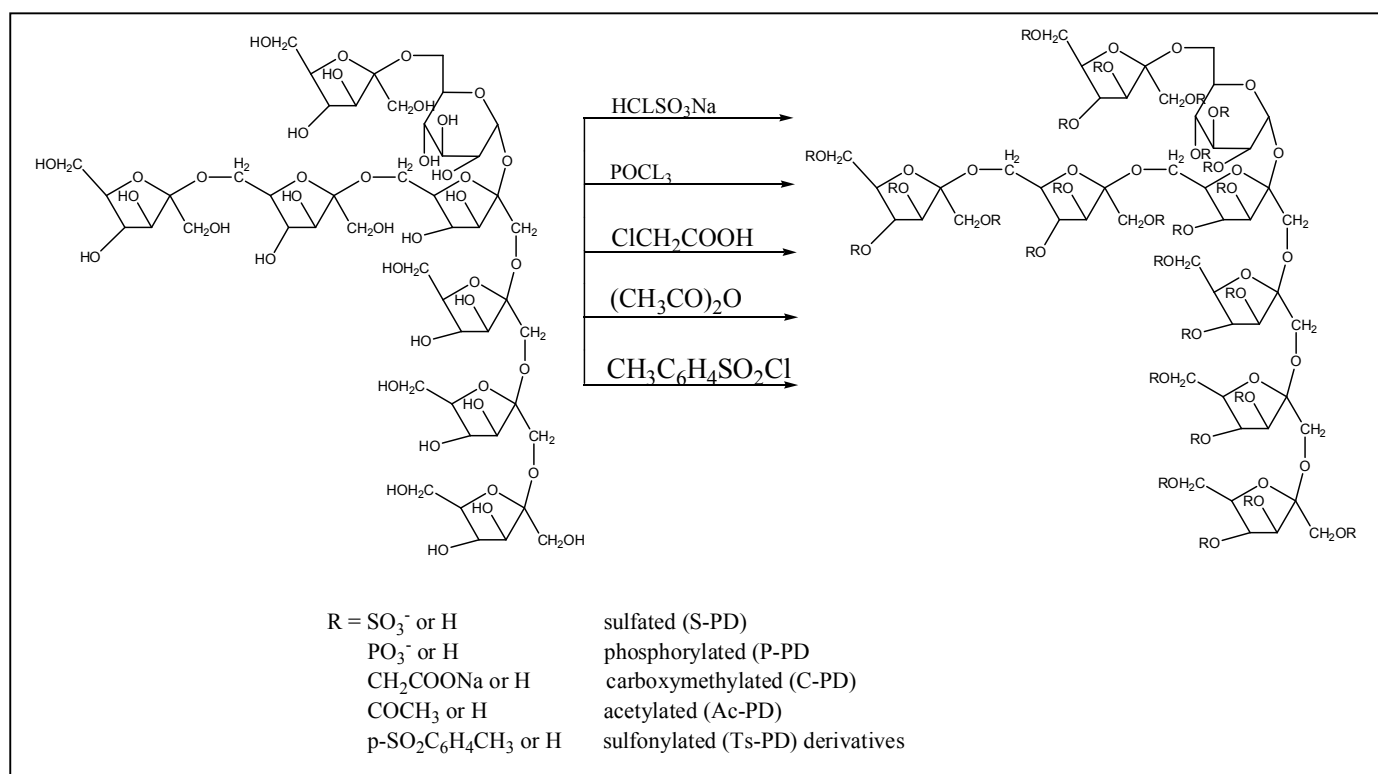
1. $R_1 = R_2 = R_3 = H$
2. $R_1 = Ac, R_2 = R_3 = H$
3. $R_1 = R_3 = H, R_2 = Ac$
4. $R_1 = R_2 = H, R_3 = Ac$

1. (3b,23S,25R)-23-(α -l-Arabinopyranosyloxy)spirost-5-en-3-yl 4-O-(6-Deoxy- α -l-mannopyranosyl)-d-glucopyranoside (Polypunctoside-A).
2. (3b,23S,25R)-23-[(2-O-acetyl- α -l-arabinopyranosyl)oxy]spirost-5-en-3-yl 4-O-(6-Deoxy- α -l-mannopyranosyl)-d-glucopyranoside (Polypunctoside).
3. (3b,23S,25R)-23-[(3-O-acetyl- α -l-arabinopyranosyl)oxy]spirost-5-en-3-yl 4-O-(6-Deoxy- α -l-mannopyranosyl)-d-glucopyranoside (Polypunctoside).
4. (3b,23S,25R)-23-[(4-O-acetyl- α -l-arabinopyranosyl)oxy]spirost-5-en-3-yl 4-O-(6-Deoxy- α -l-mannopyranosyl)-d-glucopyranoside (Polypunctoside).

Interestingly, the glycosides may be regarded as internal acetate. Glycosides are found to exert a wide spectrum of therapeutic actions, both in modern medicines and in traditional medicaments, ranging from cardiotoxic, analgesic, purgative, and anti-rheumatic, demulcent and host of other useful actions (Ashutosh Kar, 2007).

Carbohydrates

Carbohydrates belong to the chemical class of the aldehydes, ketone alcohols and also the condensation polymers of these partially oxidized polyalcohols collectively known as 'Polysaccharides' or 'Oligosaccharides'.



Nevertheless, the starch and sugars find their abundant applications not only as food or food supplements, but also as indispensable adjuvants in the formulation of a wide range of pharmaceutical products all over the globe (Ashutosh Kar, 2007).

Fatty acids

A single plant active on its own is often worthless and the entire plant usually works far better than any of its single components. Plant oil produced from seeds and fruit kernels are a rich source of fatty acids which provide emolliency, hydrophobicity and skin protection from the drying effects of wind and sun. As little as 2-5% of any fixed oil will provide protection to the skin and help prevent the loss of hydration for the stratum corneum and underlying tissue. In addition to these materials one finds other materials which perhaps offer more than simple protection. These materials are gamma-linolenic acid (GLA), linoleic acid and other complex molecules (Anthony C D, 2003).

Pharmacognostic studies of *Polygonatum* species

Polygonatum grows on hills, a shrub higher than a foot, with leaves similar to laurel but broader and smoother, somewhat similar in taste to a quince or pomegranate, for it tastes astringent. At every emerging of the leaves are white flowers in a larger quantity than the leaves, the number to

be reckoned from the root. It has a white root; soft, long, with many thick joints, strongly scented the thickness of a finger — good applied on wounds, and to take away spots on the face.

The rhizomes of *Polygonatum cirrifolium* and *Polygonatum verticillatum* are well known as members of “Ashtavarga” a group of eight drugs in the Ayurvedic system of medicine, and highly valued for their rejuvenating, restorative and activating effect. These two species of *Polygonatum* can be differentiated from each other on the basis of colour, size, microscopy and HPTLC fingerprint profile. Dried rhizomes of *P. cirrifolium* are cream colored and smooth surfaced, about 0.4-0.8 cm broad while *P. verticillatum* rhizomes are orange-brown in color, rough or sandy surfaced and 1-2 cm broad. Histologically the rhizomes are similar in both species but the roots show sclerenchymatous central zone in *P. verticillatum* that is absent in *P. cirrifolium*. Steroidal saponins are detected in both species (Pandey et al., 2006).

Pharmacological activities

Plants have always been an attractive source of drugs. Nevertheless, intricate ways of molecular interactions and bioactivity mechanisms of the extracts or their bioactive constituents provide a challenge to the scientists (Colegate et al., 2008). Plants of the genus *Polygonatum* display a wide

range of pharmacological activities. A brief overview of their activities has been presented here.

Aphrodisiac activities

Kazmi I. et al., (2012) and Rana C.S. (2012) reported that the effect of *Polygonatum verticillatum* leaf aqueous extract upon the expression of male rat sexual behaviour, in order to know whether *Polygonatum verticillatum* leaf aqueous extract possess aphrodisiac property. The extract (500 mg/kg body weight/day) and L-dopa (100 mg/kg body weight/day) were administered orally by gavages for 28 days. They observed various parameters as mount latency, intromission latency, ejaculation latency, mounting frequency, intromission frequency, ejaculation frequency and post ejaculatory interval before and during the sexual behaviour study at day 0, 7, 14, 21 and 28. The *Polygonatum verticillatum* leaf aqueous extract reduced significantly ML, IL, EL and PEI ($P < 0.05$, $P < 0.01$, $P < 0.001$). The extract also increased significantly MF, IF and EF ($P < 0.05$, $P < 0.01$, $P < 0.001$). These effects were observed in sexually active and inactive male rats.

Antitherpetic activities

Liu X. et al (2011) reported that the chemically modified polysaccharides, including sulfated, phosphorylated, carboxymethylated, acetylated and sulfonylated derivatives, were prepared from a neutral polysaccharide extracted from *Polygonatum cyrtoneuma* Hua. These compounds were characterized by FT-IR, ¹H NMR and ¹³C NMR spectroscopy. Antitherpetic activities of natural and modified *P. cyrtoneuma* polysaccharide against herpes simplex virus induced by cyclophosphamide were then evaluated on vero cells using cytopathic effect inhibition assay.

Antimalarial and free radical scavenging activity

Khan H. et al., (2011) reported that the antimalarial activity of the crude extract of *Polygonatum verticillatum* rhizomes and its sequentially partitioned fractions were investigated against *Plasmodium falciparum*. The crude extract possessed notably activity (IC_{50} : 21.27 μ g/mL) and enhanced reasonably upon fractionation. The antiparasitic potency of the n-hexane fraction was maximum (IC_{50} : 2.23 μ g/mL) followed by chloroform (IC_{50} : 4.62 μ g/mL).

Also the extracts of the plant showed marketed scavenging activity on stable free radical, DPPH. The most potent antioxidant was the chloroform fraction (IC_{50} : 90 μ g/mL)

followed by ethyl acetate (IC_{50} : 93 μ g/mL) and n-butanol (IC_{50} : 95 μ g/mL) fractions.

Antimicrobial activities:

Khan H. et al., (2012) reported that the Antimicrobial activity of the rhizomes of *Polygonatum verticillatum* against various pathogenic bacteria and fungi. Broad spectrum antibacterial activity was demonstrated by the crude extract of the plant and its subsequent solvent fractions; predominantly against Gram-negative bacteria. MICs of the extracts against *Escherchia coli*, *Salmonella typhi* and *Shigella flexeneri* were in the range of 1.5-40 g/ml, 03-06 g/ml and 03-40 g/ml, respectively. The only sensitive Gram-positive bacterium was *Staphylococcus aureus* with MICs in the range of 75-80 g/ml. The fungicidal activity was limited to *Microsporum canis* and *Fusarium solani* and the MICs were in the range of 350-360 g/mL and 190-290 g/ml respectively. The various fractions of rhizomes contained significant concentration of total flavonoidal and total phenolic contents that could be responsible for the current findings.

Antipyretic and Anticonvulsant Activity

Khan H. et al., (2012) reported that the study was undertaken to explore the antipyretic and anticonvulsant profile of the *Polygonatum verticillatum* in established pharmacological paradigms. The crude methanol extract of rhizomes (PR) and aerial parts (PA) of the plant were tested in Brewer's-yeast-induced pyrexia and pentylenetetrazole-induced convulsion test. PR and PA both evoked prominent antipyretic activity ($p < 0.01$) in a dose-dependent manner during all assessment times at the dose of 50, 100, and 200 mg/kg intraperitoneally. The protection elicited by PR (82.20%) at 200 mg/kg was comparable with aspirin (88.48%) as a standard drug at 100 mg/kg. However, PA was less potent, and maximum protection was 64% at 200 mg/kg. Both PR and PA were devoid of any anticonvulsant activity. Our results demonstrated prominent evidence of antipyretic activity of *P. verticillatum* that is consistent with the folk uses of the plant. In addition from a biodiversity point of view, PA of the plant can also be used as an alternate of PR.

Antinephrotic activity

Chunhua Z et al., (2011) reported that the Huang I Haul (HQH) granules, a mixture of Chinese herbs, contain teammate's robinophila murr, wolfberry fruit, and

Polygonatum. We investigated the mechanism of the protective effects of HQH on Adriamycin nephrosis (ADR) in rats. Adriamycin nephrotic rats were induced by a single dose of 5 mg/kg Adriamycin. For the HQH-treated Adriamycin nephrosis group, 1 day after treatment with 5 mg/kg Adriamycin, the rats were administered once-daily oral gavage of 2 mg/kg HQH for 15 days. All the rats were killed at day 15. Histological changes were observed by light microscopy and transmission electron microscope. Nephron and podocyte expression levels were measured by real-time RT-PCR and Western blot. ADR rats showed heavy proteinuria, podocyte and tubulointerstitial injury, macrophage infiltration, and increased levels of serum cytokines TNF- α and IL-1 β . HQH significantly ameliorated the adriamycin-induced renal injury. These data were validated in the cultured podocytes. The podocytes were treated by Adriamycin in the presence or absence of HQH and nephron and podocyte expression and TNF- α and IL-1 β synthesis and secretion were determined by real-time RT-PCR, immunoblotting, and ELISA, respectively. Adriamycin significantly reduced nephron and podocyte expression, which was significantly restored by the treatment of HQH. HQH treatment inhibited adriamycin-induced TNF- α and IL-1 β expression. Our findings suggest that HQH significantly reduces proteinuria, prevents podocyte injury, and ameliorates tubulointerstitial damage. Inhibition of inflammatory cytokine expression and macrophage infiltration may be the protective mechanism of HQH.

Antineoplastic activities:

Wang S et al., (2011) reported that the *Polygonatum cyrtoneum* lectin (PCL), a mannose/sialic acid-binding plant lectin, has recently drawn a rising attention for cancer biologists because PCL bears remarkable anti-tumor activities and thus inducing programmed cell death (PCD) including apoptosis and autophagy in cancer cells. PCL induces cancer cell apoptotic death such as the caspase-dependent pathway, mitochondria-mediated ROS-p38-p53 pathway, Ras-Raf and PI3K-Akt pathways. In addition, we further elucidate that PCL induces cancer cell autophagic death via activating mitochondrial ROS-p38-p53 pathway, as well as via blocking Ras-Raf and PI3K-Akt pathways, suggesting an intricate relationship between autophagic and apoptotic death in PCL-induced cancer cells.

Antinociceptive activity

Khan H, (2010) reported that the crude methanolic extract of the rhizomes of *Polygonatum verticillatum* (PR) was tested in various established pain models in rodents at 50, 100 and 200 mg/kg i.p. while the diuretic activity was assessed at 300 and 600 mg/kg p.o. in rats. PR demonstrated significant reduction (14–72%) in the number of writhes induced by acetic acid in a dose-dependent manner. When nociceptive threshold was measured in the formalin test, PR strongly attenuated the formalin-induced flinching behavior in both phases (6–30% in first phase while 12–72% in second phase). Central involvement in the analgesic profile of PR was confirmed by the hot plate test, in which PR elicited a significant ($P < 0.01$) analgesic activity by increasing latency time. However, an opioid receptor antagonist, naloxone (2 mg/kg s.c.) strongly antagonized the antinociceptive activity of PR.

Antityrosinase activity

Yan Y. (2010) and Khan H. (2012) reported that the tyrosinase inhibitors are becoming increasingly important in controlling skin hyperpigmentation. We aimed to screen 50 extracts from traditional Chinese medicines (TCM) for tyrosinase activity-inhibiting agents. In the cell-free assay, 10 out of the 50 extracts demonstrated more than 50% inhibition against mushroom tyrosinase activity. These 10 extracts were further assessed by cellular tyrosinase assay, and 6 showed > 50% inhibition with IC₅₀ values <1 mg/ml. The 6 extracts are from 3 herbs namely *Ampelopsis japonica*, *Lindera aggregata*, and *Polygonatum odoratum* and 3 formulas namely Qian-wang-hong-bai-san, Qiong-yu-gao, and San-bai-tang. As compared with vitamin C, these 6 extracts showed similar or greater ratio of cell growth IC₅₀ to cellular tyrosinase IC₅₀. As compared with arbutin, extract from *Ampelopsis japonica*, *Lindera aggregata*, Qian-wang-hong-bai-san, or San-bai-tang had a similar, although extract from *Polygonatum odoratum* or Qiong-yu-gao had a greater, IC₅₀ value against murine tyrosinase activity.

Antibacterial and antifungal activity

Wang Y F et al., (2003) reported that the *Polygonatum kingianum* Coll. Et Hemsl. (Liliaceae) is mainly distributed in south western China. Its rhizome called “Huang-jing” is widely used in traditional Chinese medicine as a tonic and a remedy to treat lung disease, upset stomach and diabetes. A new

indolizinone, namely kinganone together with 3-ethoxymethyl-5, 6, 7, 8-tetrahydro-8-indolizinone and isomucronutol were isolated from the rhizomes of *Polygonatum kingianum*. Their structures were elucidated mainly on the basis of spectral data. Indolizinone show weak antibacterial and antifungal activity with compared to rifampicin and amphotericin respectively, in the agar diffusion method.

Cytotoxicity

Li X.C. et al. (1992) and Yang Q.X. et al., (2006) reported four new steroidal saponins, polypunctosides A–D (1–4, resp.), were isolated from the rhizomes of *Polygonatum punctatum*, together with five known steroidal saponins. On the basis of chemical and spectral evidence, the structures of the new saponins were established as (3b,23S,25R)-23-(α -larabinopyranosyloxy) spirost-5-en-3-yl 4-O-(6-deoxy- α -l-mannopyranosyl)-d-glucopyranoside (1), (3b,23S,25R)-23-[[2-O-acetyl- α -l-arabinopyranosyl]oxy]spirost-5-en-3-yl 4-O-(6-deoxy- α -l-mannopyranosyl)-d-glucopyranoside (2), (3b,23S,25R)-23-[[3-O-acetyl- α -l-arabinopyranosyl]oxy]spirost-5-en-3-yl 4-O-(6-deoxy- α -l-mannopyranosyl)-d-glucopyranoside (3), and (3b,23S,25R)-23-[[4-O-acetyl- α -l-arabinopyranosyl]oxy]spirost-5-en-3-yl 4-O-(6-deoxy- α -l-manno-pyranosyl)-d-glucopyranoside (4). The cytotoxic activity of the isolated saponins was evaluated towards HeLa cells.

Saeed M. et al., (2010a) reported that the concentration of various micronutrients using atomic absorption spectrophotometer and macronutrients using flame photometry and evaluation of cytotoxicity of the aerial parts of the *Polygonatum verticillatum*. Based on the results, the crude extract and its various fractions contained marked concentrations of both micronutrients and macronutrients. The predominant micronutrients were Zn, Fe, Cu, Mn, Cr and Ni. It was noticeable that Ni concentration in hexane (1.80 ppm) and ethyl acetate (2.40 ppm) fractions were beyond the permissible limit (1.5 ppm) for plants and Zn concentration in butanol fraction (60 ppm) was also beyond the permissible limit for plants (50 ppm). Outstanding concentrations of macronutrients were possessed by all solvent fractions with Ca, Na and K ranges from 100–220 ppm, 120–560 ppm and 2500–3400 ppm respectively. There was no sign of brine shrimp cytotoxicity except in the chloroform fraction

(LD50 was 1205.07 g/mL). It is concluded that the aerial parts of the plant could be a significant source of micro and macro nutrients without significant cytotoxicity and thus this study validated the folkloric use of the plant as a tonic and energizer.

Insecticidal activity

Saeed M et al., (2010a) reported that the aerial parts of the *Polygonatum verticillatum* for biological activities such as phytotoxic, insecticidal and leishmanicidal properties. Outstanding phytotoxicity was observed for the crude extract and its subsequent solvent fractions against *Lemna acquinotialis* Welw at tested doses of 5, 50 and 500 mg/ml. Complete growth inhibition (100%) was demonstrated by the crude extract and aqueous fraction at maximum tested dose (500 mg/ml). Among the tested insects; moderate insecticidal activity was recorded against *Rhyzopertha dominica*. However, neither crude extract nor its solvent fraction registered any significant (> 100 mg/ml) leishmanicidal activity against *Leishmania major*. Based on the phytotoxicity, the aerial parts of the plant could be a significant source of natural herbicidal for sustainable weed control.

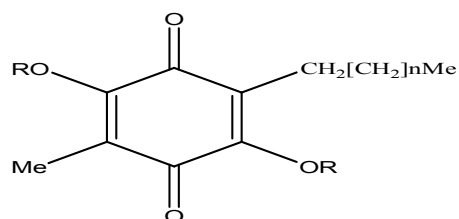
Respiratory diseases

Choong J. L. (2004) reported that the *Polygonatum odoratum* are used for the treatment of respiratory diseases in oriental medicine and their respective components were reported to have various biological effects. In this study, we investigated whether these natural products affect mucin release from cultured hamster tracheal surface epithelial cells and compared the possible activities of these agents with the inhibitory action on mucin release by poly-L-lysine and the stimulatory action by adenosine triphosphate. Confluent primary hamster tracheal surface epithelial cells were metabolically radio labeled using ^3H -glucosamine for 24 h and treated for 30 min in the presence of varying concentrations of each agent to assess the effects on ^3H -mucin release. They studied that betaine and hesperidin can increase mucin release by direct acting on airway mucin-secreting cells and suggest these agents be further studied for the possible use as mild expectorants during the treatment of chronic airway diseases.

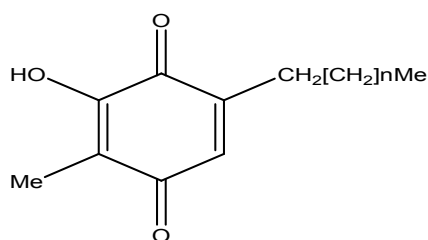
Miscellaneous activity

Dried root of *Polygonatum multiflorum* Thunb. (Polygonaceae), well known as Hersouwu, is one of the most

popular traditional medicinal herbs in Taiwan. It is frequently used to treat weakness, backache, knee pain, premature graying of hair in traditional Chinese medicine (Zhao Z, 2004). *Polygonatum multiflorum* has been used for a long time as an antiaging agent and possesses hypocholesterolemic, antitumor and vasorelaxant effects (Zhang et al., 1983; Xiao et al., 1993). Its water extract exhibits a variety of pharmacological effects such as a preventive effect against cognitive deficits induced by A β 25–35 in mice (Um et al., 2006), antioxidative action (Chiu et al., 2002), free radical scavenging effect, the inhibition of monoamine oxidase (MAO) activity (Yang X, 1996), improving memory (Chan et al., 2003), etc. The main active constituents of the herb have been reported to be hydroxyanthraquinones, stilbenes, phenolic compounds and their glycosides, etc. (Zheng et al., 1997). Emodin (1, 3, 8-trihydroxy-6-methylanthraquinone), an anthraquinone derivative from *Hersowu* (*Polygonatum multiflorum* Thunb.), has protective effect against brain disturbances induced by severe cerebral injury (Gu et al., 2003). Emodin has been shown to inhibit lipid peroxidation in rat brain homogenates (Sato et al., 1992).



2,5-di-alkyl-3,6-dihydroxy-p-benzoquinone



2-hydroxy-3-methyl-6-alkyl-1,4-benzoquinone

Polygonatum odoratum lectin (POL), a novel mannose-binding lectin with anti-viral and apoptosis inducing activities, was isolated from rhizomes of *Polygonatum odoratum* (Mill.) Druce. POL was a homo-tetramer with molecular weight of 11953.623 Da per subunits as determined by gel filtration, SDS-PAGE and mass spectrometry. Based on its N-terminal

29-amino acid sequence the full-length cDNA sequence of POL was cloned. Subsequent phylogenetic analysis and molecular modeling revealed that POL belonged to the *Galanthusnivalis* agglutinin (GNA)-related lectin family, which acquired unique mannose-binding specificity. The hem agglutinating activities of POL were metal ion-independent, and were stable within certain range of pH and temperature alterations. Moreover, POL showed remarkable anti-HSV-II activity towards Vero cells, cytotoxicity towards human melanoma A375 cells and induced apoptosis in a caspase-dependent manner.

Conclusion

The following manifestations can be made on the basis of this comprehensive perusal of literature, that the plants of genus *Polygonatum* are being used traditionally, due to their immense therapeutic potential to treat/cure various diseases. Phenolics and triterpenes are present in plants and exhibit significant biological activity. Many studies demonstrated significant anti-inflammatory activity of the extracts and some isolated constituents obtained from the plants of this genus. This vindicated the use of certain species in the chronic and acute inflammatory diseases including psoriasis, dermatitis and other skin disorders. A variety of phytoconstituents has been isolated from the different species of the genus *Polygonatum*. However, only a few species have been explored exhaustively for their chemical constituents and pharmacological activities.

Thus, there remains a tremendous scope for further scientific exploration of this genus, to establish their therapeutic efficacy and commercial exploitation.

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REFERENCES

1. Adams M, Francine G, Hamburger M. (2003) *Journal of Ethnopharmacology*. 113:363–381.
2. Ahn M J, Kim C Y, Yoon K D. (2006) *J Nat Prod*. 69:360–364.
3. Alluri V K, Tayi V N R, Dodda S, Mulabagal V, Hsin-Sheng T, Gottumukkala V S, (2006) *Int J App Sci Eng*. 4:115–125.
4. Anthony C D. (2003) *Australian Society of Cosmetic Chemists Annual Congress*, Hamilton Island. p. 4.
5. Antoniuk V. (1993) *Ukr Biokhim Zh*. 65: 41–48.

6. Ashutosh Kar, (2007). Pharmacognosy and Pharmacobiotechnology. Published by New Age International (P) Ltd., Publishers, New Delhi-110002. P. 84–374.
7. Ayres D C, Loike J D. (1990). Lignans: Chemical, biological and clinical properties. Press syndicate of the University of Cambridge, Cambridge.
8. Balkrishna A, Shrivastava A, Mishra R K, Patel S P, Vashistha RK, Singh A, Jadon V, Saxena P. (2012) Int. J. Med. Arom. 2(4): 661-676
9. Bisht C, Badoni A. (2009) New York Science Journal. 2(5):1554-0200.
10. Chan Y C, Wang M F, Chang H C. (2003) American Journal of Chinese Medicine. 31: 171–179.
11. Chiu P Y, Mak, D H, Poon M K, Ko K M, (2002). *Planta Medica* 68:951–956.
12. Choi SB and Park S (2002). A steroidal glycoside from *Polygonatum odoratum* (Mill.) Druce. Improve insulin resistance but does not alter insulin secretion in 90% pancreatectomized rats. *Biosci Biotechnol Biochem* 66, 2036-2043.
13. Choong J L, Jae H L, Jeong H S, Gang M H, Ji P, Sohyun B, Jong H L, Yang C P. (2004) *Phytother. Res.* 18:301–305.
14. Chun N L, Pao L H, Chai M L, Ru R W. (1997) *Tetrahedron*, Vol. 53(6): 2025-2028.
15. Chunhua Z, Huang S, Ding G, Yuan Y, Chen Q, Pan X, Chen R, Zhang A. (2011) *Pediatr Nephrol.* 26:905–913.
16. Colegate S M, Molyneux R J (2008) CRC Press Tylor and Francis Group, pp. 1-100.
17. Fen L, Yinghua L, Yiwen M, Min Y, Kaize H (2004) *Antiviral Research.* 63: 183–189.
18. Gao H, Huang Y-N, Gao B, Li P, Inagaki C and Kawabata J (2008) Inhibitory effect on alphasglucosidase by *Adhatoda vasica* Nees. *Food Chemistry* 108, 965-972.
19. Gu H M, Meng Y W, Pu Q. (2003). *Chinese Journal of Applied Environmental Biology.* 9(1):21–23.
20. Hai L Q, Zhihong L I, Peng W. (2003). *Chinese Chemical Letters.* 14 (12): 1259-1260.
21. Harborne J B, Baxter H, Moss G P. (1999). *Phytochemical dictionary: A handbook of bioactive compounds from plants.* Tylor & Francis Ltd., London, p. 773.
22. Harborne J B, Mabry T J, Mabry H (1975). *The Flavonoids.* Academic Press, New York, pp. 1-40.
23. Heber D. (2004). *Journal of Postgraduate Medicine.* 50:145–149.
24. He-Shui Y, Bai-Ping M, Xin-Bo S, Li-Ping K, Tao Z, Jing F, Yang Z, Cheng-Qi X, Da-Wei T, Li-Juan Z, Jie Z, Kate Y. (2010) *Helvetica ChimicaActa.* 93.
25. Humphrey A J, Beale M H (2006). *Terpenes: Plant secondary metabolites: occurrence, structure and role in the human diet.* Crozier A, Clifford MN, Ashihara H. (Ed). Blackwell publishing company, Oxford, p. 47.
26. Ibrar M, Muhammad M, Barkatullah, Khan H, Jahan F, Ashraf N. (2012) *Phytopharmacology.* 3(1):191-198.
27. Jiang S, (1977) *The Dictionary of Chinese Herbal Medicines.* Shanghai People's Publishing Press, Shanghai, pp. 2041–2044.
28. Jiang S, (1986). *Dictionary of Chinese Medicine.* Shanghai Press of Science Technology, pp. 551–553.
29. Kazmi I, Afzal M, Rahman M, Gupta G, Anwar F. (2012) *Asian Pacific Journal of Tropical Disease.* S841-S845.
30. Kennedy R O, Thornes R D (1997). *Coumarins: biology, applications and mode of action.* Willy publication, pp. 1.
31. Khan H, Saeed M, Gilani A H, Khan M A, Khan I, Ashraf N (2011) *Phytotherapy Research* 25:1024-1030
32. Khan H, Saeed M, Khan M A, Haq I, Muhammad N, Ghaffar R. (2012) *Journal of Medicinal Chemistry Research.* 12: 0194-198
33. Khan H, Saeed M, Khan M A, Khan I, Ahmad M, Muhammad N, Khan A. (2011) *Med Chem Res.* 20: 00044-011-9637.
34. Khan H, Saeed M, Muhammad M, Ghaffar R, Khan S A, Hassan S. (2012) *Pak. J. Pharm. Sci.* 25(2):463-467.
35. Khan H, Saeeda M, Gilani A, Khan M, Dar A, Khan I (2010). *Journal of Ethnopharmacology* 127:521–527.
36. Khan H, Saeed M, Gilani A H, Muhammad N, Haq I U, Ashraf N, Rehman N U, Haleemi A. (2012) *Phytother Res.*
37. Khan S W, Khatoon S. (2008) *Pak. J. Bot.* 40(1):43-58
38. Kramp K, Huck S, Niketic M, Tomovic G, Schmitt I. (2009) *Plant Biol (Stuttg).* 11(3):392-404
39. Li X C, Yang C R, Makoto I, Hiromichi M, Ryoji K, Kazuo Y. (1992) *Phytochemistry.* 31(10):3559–3563.
40. Liu B, Cheng Y, Zhang B, Bian Hj and Bao Jk (2009a) *Polygonatum cyrtanema* lectin induces apoptosis and autophagy in human melanoma A375 cells through a mitochondria-mediated ROS-p38-p53 pathway. *Cancer Letters* 275, 54-60.
41. Liu B, Peng H, Yao Q, Li J, Van Damme E, Balzarini J and Bao Jk (2009). Bioinformatics analyses of the mannose-binding lectins from *Polygonatum cyrtanema*, *Ophiopogon japonicus* and *Liparis novversa* with antiproliferative and apoptosis-inducing activities. *Phytomedicine* 16, 601-608.
42. Liu B, Zhang B, Min Mw, Bian Hj, Chen L, Liu Q and Bao Jk (2009b). Induction of apoptosis by *Polygonatum odoratum* lectin and its molecular

- mechanisms in murine fibrosarcoma L929 cells. *Biochimica et Biophysica Acta (BBA) - General Subjects* 1790, 840-844.
43. Liu L, Qun D, Xiao-tang D, Ji-nian F, Kan D. (2007) *Carbohydrate Polymers* 70:304–309.
 44. Liu X, Zhen-jiang W, Lin S, Xiao-xia L. (2011) *Carbohydrate Polymers* 83:737–742.
 45. McClure J W (1986). Physiology of flavonoids in plants. In: *Plant flavonoids in biology and medicine: Biochemical, pharmacological, and structure-activity relationships*. Cody V, Middleton E, Harborne J B. (Ed). Alan R. Liss, Inc. New York, pp. 77-85.
 46. Memnune S, Hilalyildiz, N G, Bulent C, Zeynep E, Sezai E. (2009) *Pak. J. Pharm. Sci.* 22(1):102-106.
 47. Mi-Jeong A, Chul Y K, Kee-Dong Y, Min Y, Jong HC, Young WC, Jinwoong K. (2006) *J. Nat. Prod.* 69:360-364.
 48. Ming-Chin L, Ming-Tsuen H, Chi-Rei W, Hao-Yuan C, Chia-Chang H, Yao-Tung L, Wen-Huang P. (2007) *Journal of Ethnopharmacology.* 112:552–556.
 49. Mohamed M R, Bret C V. (2007) *Food Chemistry* 104:332–340.
 50. Muhammad S, Haroon K, Murad A K, Shabana U S, Naveed M, Saeed A K. (2010) *African Journal of Biotechnology.* 9(8):1241-1244.
 51. Pandey M M, Govindarajan R, Khatoon S, Rawat A K S, Mehrotra S. (2006) *Journal of Herbs, Spices & Medicinal Plants,* 12:01-02
 52. Pao L H, Kim H G, Ru R W, Chun N L. (1997) *Phytochemistry.* 44 (7): 1369-1373.
 53. Paul M D. (2002) *Medicinal Natural Products: A Biosynthetic Approach*, 2nd ed. p. cm. Publisher John Wiley & Sons, Inc., 605 Third Avenue, New York, NY 10158-0012, USA, pp. 232.
 54. Quin Y, Jing Y L, Wei Q, Yan Y C. (2010) *Chinese Chemical Letters* 21:706–708.
 55. Rana C S, Tiwari J K, Dangwal L R, Sundriyal R C. (2012) *Indian Journal of traditional knowledge.* 11(4):646-651.
 56. Saeed M, Khan H, Khan M A, Khan F, Khan S A , Muhammad N. (2010) *Pak. J. Bot.* 42: 3995-4002.
 57. Sato H, Ishizawa F, Hirayama H, Hishinuma T, Mizugaki M. (1992) *Yakugaku Zasshi* 112:199–202.
 58. Sharma P K, Chauhan N S, Lal B. (2004) *Journal of Ethnopharmacology.* 92:167–176.
 59. Shuli M, Wen Y G, Yan J Z, Luqi H, Chang X L. (2010) *Fitoterapia* 81:703–714.
 60. Singh A P (2006). *Ethnobot. Leaflets.*10:104-108.
 61. Srivastava B, Sinha A, Jadhav A D, Meena A K, Mehta H C, Gupta M D (2012) A review on Phytochemistry, Pharmacology, Folklore Claims, and Ayurvedic Studies of *Polygonatum verticillatum*. 04(6):0975-4407.
 62. Tamura M N. (1993). *Botanische Jahrbücherfür Systematik* 115:01–26.
 63. Um M Y, Choi W H, Aan J Y, Kim S R, Ha T Y. (2006) *Journal of Ethnopharmacology* 104:144–148.
 64. Wang S, Qi-jiā Y, Jin-ku B, Bo L. (2011) *Biochemical and Biophysical Research Communications.* 406:497–500.
 65. Wang Y F, Chun H L, Guo F L, Jian X C, Shi D L. (2003) *Planta Med.* 69:1066-1068.
 66. Wei D, Hai B S, Heng M, Yan B M, Tong J L, and Wei W. (2010) *Arch Pharm Res.* 33(5); 669-674.
 67. Xia S, Yun G, Qing D S. (2006) *Flavour Fragr. J.* 21: 556–558.
 68. Xiao P G, Xing, S T, Wang, L W, (1993) *Journal of Ethnopharmacology* 38:167–175.
 69. Yan Y, Gui-Xin C, Dan-Dan M, Hui W, Jian-Hong C, Alexander K L, Wang-fun F, Zhi-Ling Y. (2010) *Journal of Ethnopharmacology* 129:387–390.
 70. Yang Q-X, Yang C-R. (2006) *Chemistry and Biodiversity* 3:1349-1355.
 71. Yang X, (1996). *Zhongguo Zhong Yao Za Zhi* 21:48–49.
 72. Yang Y, Huai L X, Zi T Z, Jun J L, Wen W L, Hua M, Jin K B (2011) *Phytomedicine* 18:748–755.
 73. Ying W, Yim H C, Zhiqi Y, Jen F C, Chi M C, Qing Y H. (2006) *Proteomics.* 6:2422–2432.
 74. Yu H, Ma B, Kang L, Zhang T, Jiang F, Zhang J, Zou P, Zhao Y, Xiong C and Tan D (2009) *Chemical and Pharmaceutical Bulletin.* 57:1011-1014.
 75. Zeng G F, Zhi-yong Z, Li L, De-qiang X, Chun-xiang X, Yu-xi Z, Shao-hui Z (2011) *Journal of Ethnopharmacology.* 136:224–229.
 76. Zhang Z, Zhuang Q Q, Mei M Z, (1983) *Yao Xue Xue Bao* 18:468–471.
 77. Zhao ZZ: “An Illustrated Chinese Materia Medica in Hong Kong”. Chung Hwa Book Co., Ltd., Hong Kong, pp. 307–308, 2004,.
 78. Zheng H Z, Dong Z H, Se J. (1997) *Journal of Fermentation and Bioengineering.* 84:378–381.
 79. Zi T Z, Hao P, Chun Y L, Jun J L, Ting T Z, Yi F Y, Yan L, Jin K B. (2010) *Phytomedicine* 18:25–31.