Chemical and Pharmacological Researches on *Hyoscyamus niger*

LI Jun[1], SHI Ji[2], YU Xin-wen[2], SUN Jing-kuan[3], MEN Qi-ming[1*], KANG Ting-guo[2*]

1. Dalian Institute for Food and Drug Control, Dalian 116021, China
2. College of Pharmacy, Liaoning University of Traditional Chinese Medicine, Dalian 116023, China
3. The Second Affiliated Hospital of Dalian Medical University, Dalian 116023, China

Abstract: The reports on chemical constituents of *Hyoscyamus niger* were summarized. The compounds include alkaloids, saponins, lignans, coumarinolignans, flavonoids, and some other nonalkaloidal compounds. TLC, HPLC, and GC were used for the qualitative and quantitative analyses of some chemical constituents in *H. niger*. Modern pharmacological experiments showed that *H. niger* had the analgesic, anti-inflammatory, antipyretic, anticonvulsant, spasmolytic, antidiarrhoeal, antisecretory, bronchodilatory, urinary bladder relaxant, hypotensive, cardiosuppressant, vasodilator, antitumor, and feeding deterrent properties. In addition, the toxicities of this medicinal plant were also described.

Key words: alkaloids; coumarinolignans; flavonoids; *Hyoscyamus niger*; lignans; saponins

DOI: 10.3969/j.issn.1674-6384.2011.02.006

Introduction

Henbane (*Hyoscyamus niger* L.), known as *Tianxianzi* in China, is a biennial herb indigenous to Europe, Western and Northern Asia, and Northern Africa. It has been introduced to Eastern Asia, North America, and Australia, and cultivated in several other countries (Gruenwald, Brendler, and Jaenicke, 2004; Spinella, 2001). It is well-known for its traditional use as a hallucinogen. This species grows to a height of 1－2.5 feet (0.3－0.7 m) and has grayish-green leaves, white (or faintly yellow) flowers with purplish veins, and dark gray seeds. The plant has a distinctly unpleasant smell, hence its folk names were Stinking Nightshade and Stinking Roger (Prance and Nesbitt, 2005). In China, the dried seeds are always used for clinic (Pharmacopoeia Committee of P. R. China, 2010). But in some authorized publications, such as *British Pharmacopoeia* (British Pharmacopoeica Committee, 2010), *British Herbal Pharmacopoeia* (British Herbal Medicine Association, 1996), and *The Complete German Commission E Monographs* (Blumenthal *et al*, 1998), the dried leaves, the flowering tops, and the whole fresh flowering plant of *H. niger* also have the medicinal use.

In China, it was initially recorded in *Shennong Herbs* (*Shennong Bencao Jing*), with the effects of relieving spasm and pain, alleviating asthma, and causing tranquilization (Pharmacopoeia Committee of P. R. China, 2010). Nowadays, it is often used as the main ingredient in some effective Chinese patent medicines. Based on the ancient Chinese monographs, it is drastically toxic.

In this review, a number of academic reports on chemistry and pharmacology of *H. niger* were consulted, which would provide a basis for further study and development of the clinical uses of this medicinal plant. It should also be reminded that the safety and control of the toxicity are as important as the effectiveness of this species.

Chemical researches

Isolation of chemical constituents

The psychoactive tropane alkaloids hyoscyamine, scopolamine, and atropine are present in all parts of the plant, but are concentrated in the seeds and roots (Nanjing University of Traditional Chinese Medicine, 2006; Prance and Nesbitt, 2005). In recent years, some non-alkaloids

* Corresponding authors: Men QM Address: Dalian Institute for Food and Drug Control, No. 888A, Huanghe Road, Shahekou District, Dalian 116021, China Tel: +86-411-8425 5200 Fax: +86-411-8425 5360 E-mail: mqm@dl.cn
Kang TG Address: Liaoning University of Traditional Chinese Medicine. No. 79, Chongshandong Road, Huanggu District, Shenyang, 110032, China Tel: +86-24-3120 7058 E-mail: kangtg@lnutcm.edu.cn
Received: August 13, 2010; Revised: November 6, 2010; Accepted: March 28, 2011
Fund: Project of the Funds for Outstanding Young Scientific Talent (2009J22DW039)

constituents, including withanolide steroids, lignanamides, tyramine derivative, steroidal saponins, glycosides, lignans, coumarinolignan, and flavonoids, were isolated and studied. The reports on chemical constituents in the seeds of *H. niger* are summarized and classified in Table 1 and Figs. 1−9. From *H. niger* leaves, rutin was ever isolated by Steinegger and Sonanini (1960).

Qualitative and quantitative analyses of *H. niger*

Qualitative and quantitative analyses of *p*-coumaric acid in *H. niger* leaves were achieved by programmed

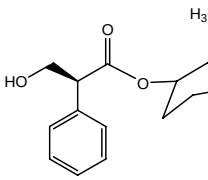
Table 1 Chemical constituents of *H. niger*

Category	No.	Compounds	References
tropane alkaloids	**1**	hyoscyamine	Nanjing University of Traditional Chinese Medicine, 2006; Prance and Nesbitt, 2005
	2	scopolamine	
	3	atropine	
withanolide class steroids	**4**	16α-acetoxyhyoscyamilactol	Ma, Williams, and Che, 1999
	5	daturalactone-4	Ma, Williams, and Che, 1999
	6	hyoscyamilactol	Ma, Williams, and Che, 1999
lignanamides	**7**	hyoscyamide	Ma, Liu, and Che, 2002
	8	grossamide	Ma, Liu, and Che, 2002
	9	cannabisin D	Ma, Liu, and Che, 2002
	10	cannabisin G	Ma, Liu, and Che, 2002
ferulic acid ester derivative	**11**	24-tetracosanediol diferulate	Ma, Liu, and Che, 2002
glycerol fatty acid ester	**12**	1-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*-nonadecanoyl glycerol	Ma, Liu, and Che, 2002
tyramine derivative	**13**	*N*-*trans*-feruloyl tyramine	Ma, Liu, and Che, 2002
longchain glycerol	**14**	1-*O*-octadecanoyl glycerol	Ma, Liu, and Che, 2002
	15	1-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol	Ma, Liu, and Che, 2002
	16	1-*O*-(9*Z*,12*Z*-octadecadienoyl)-2-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol	Ma, Liu, and Che, 2002
	17	1-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*-(9*Z*-octadecenoyl) glycerol	Ma, Liu, and Che, 2002
steroidal saponins	**18**	hyoscyamoside B	Lunga *et al*, 2008a; 2008b
	19	hyoscyamoside C	Lunga *et al*, 2008a; 2008b
	20	hyoscyamoside C_2	Lunga *et al*, 2008a; 2008b
	21	(25*R*)-5α-spirostan-3β-ol-3-*O*-β-*D*-glucopyranosyl-(1→3)-β-*D*-galactopyranoside	Lunga *et al*, 2008a; 2008b
	22	(25*R*)-5*α*-spirostan-3β-ol-3-*O*-β-D-glucopyranosyl-(1→3)-[β-*D*-glucopyranosyl-(1→2)]-β-*D*-galacto-pyranoside	Lunga *et al*, 2008a; 2008b
glycosides	**23**	hyoscyamoside A	Lunga *et al*, 2008a; 2008b
	24	hyoscyamoside B_1	Lunga *et al*, 2008a; 2008b
	25	hyoscyamoside B_2	Lunga *et al*, 2008a; 2008b
	26	hyoscyamoside B_3	Lunga *et al*, 2008a; 2008b
	27	hyoscyamoside C_1	Lunga *et al*, 2008a; 2008b
	28	hyoscyamoside E	Lunga *et al*, 2008a; 2008b
	29	hyoscyamoside F_1	Lunga *et al*, 2008a; 2008b
	30	atroposide A	Lunga *et al*, 2008a; 2008b
	31	atroposide C	Lunga *et al*, 2008a; 2008b
	32	(25*R*)-5α-spirostan-3β-ol-3-*O*-α-*L*-rhamnopyranosyl-(1→2)-β-*D*-glucopyranoside	Lunga *et al*, 2008a; 2008b
	33	(25*R*)-spirost-5-ene-3β-ol3-*O*-α-*L*-rhamnopyranosyl-(1→2)-β-*D*-glucopyranoside	Lunga *et al*, 2008a; 2008b
	34	atroposide E	Lunga *et al*, 2008a; 2008b
	35	petunioside L	Lunga *et al*, 2008a; 2008b
	36	pyranoside N	Lunga *et al*, 2008a; 2008b

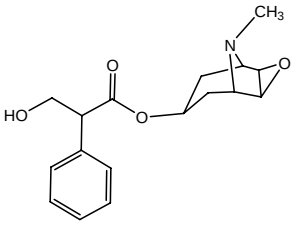
(To be continued)

(Continued Table 1)

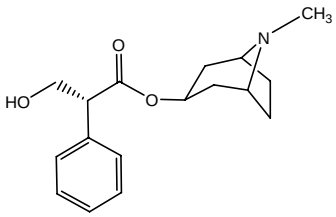
category	No.	Compounds	References
lignans	**37**	hyosmin	Begum *et al*, 2006; 2009
	38	hyoscyamal	Begum *et al*, 2006; 2009
	39	balanophonin	Begum *et al*, 2006; 2009
other compounds	**40**	rutin	Ma, Liu, and Che, 2002
	41	vanillic acid	Ma, Liu, and Che, 2002
	42	β-sitosterol	Ma, Liu, and Che, 2002
	43	daucosterol	Ma, Liu, and Che, 2002
	44	3',5-dihydroxy-3,4',5',6,7-pentamethoxyflavone	Begum *et al*, 2006; 2009
	45	(±)-pinoresinol	Begum *et al*, 2006; 2009
	46	vanillin	Begum *et al*, 2006; 2009
	47	5-hydroxymethylfurfural	Begum *et al*, 2006; 2009
glucosides	**48**	pongamoside C	Begum *et al*, 2006; 2009
	49	pongamoside D	Begum *et al*, 2006; 2009
coumarinolignans	**50**	hyosgerin	Sajeli *et al*, 2006; Begum *et al*, 2010
	51	venkatasin	Sajeli *et al*, 2006; Begum *et al*, 2010
	52	cleomiscosin A	Sajeli *et al*, 2006; Begum *et al*, 2010
	53	cleomiscosin B	Sajeli *et al*, 2006; Begum *et al*, 2010
	54	cleomiscosin A methyl ether	Sajeli *et al*, 2006; Begum *et al*, 2010
	55	cleomiscosin A-9'-acetate	Sajeli *et al*, 2006; Begum *et al*, 2010
	56	cleomiscosin B-9'-acetate	Sajeli *et al*, 2006; Begum *et al*, 2010



1 hyoscyamine

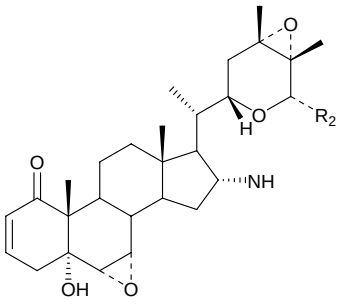


2 scopolamine



3 atropine

Fig. 1 Structures of alkaloids

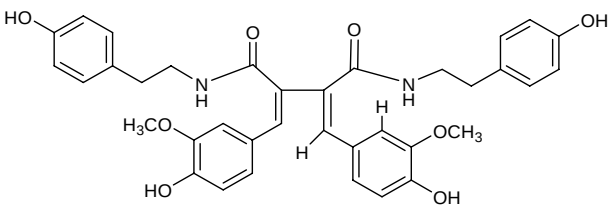


4 16α-acertoxyhyoscyamilactol R_1=OAc; R_2=α-OH, β-H

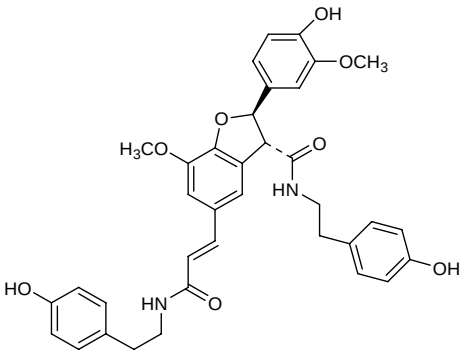
5 daturalactone-4 R_1=H; R_2=O

6 hyoscyamilactol R_1=H; R_2=α-OH, β-H

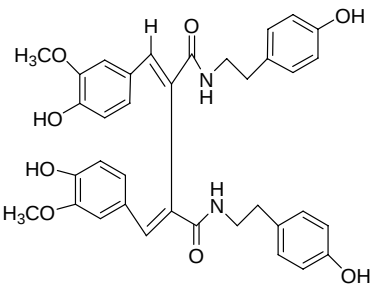
Fig. 2 Structures of withanolide class steroids



7 hyoscyamide

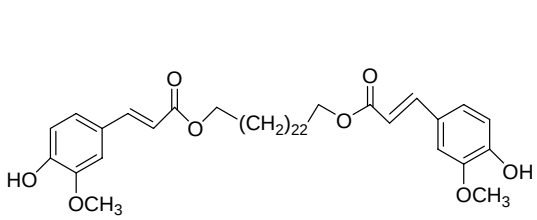


8 grossamide

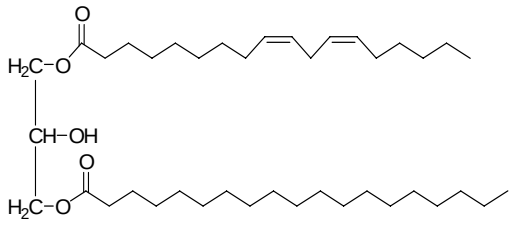


10 cannabisin G

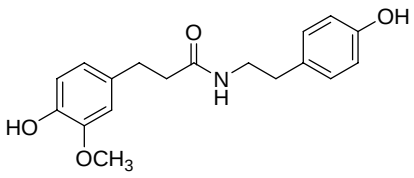
Fig. 3 Structures of lignanamides



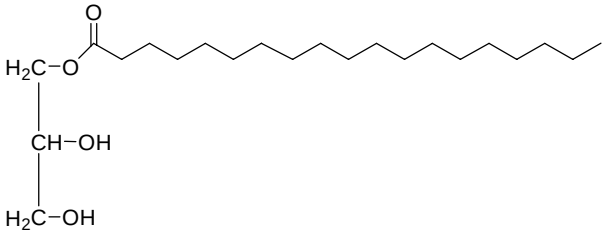
11 24-tetracosanediol diferulate



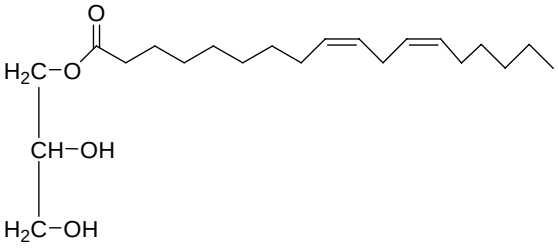
12 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*-nonadecanoyl glycerol



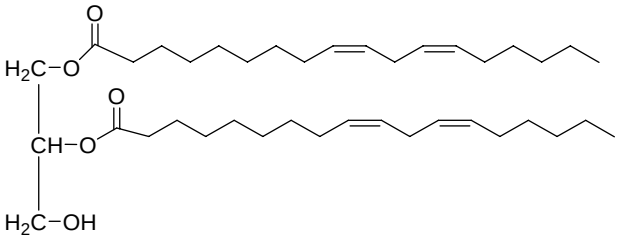
13 *N*-*trans*-feruloyl tyramine



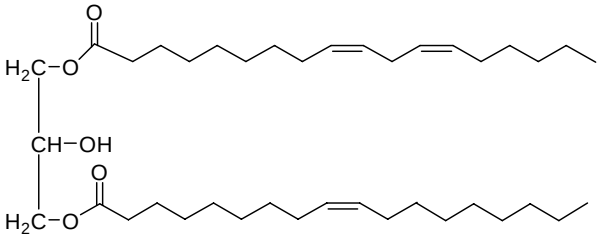
14 1-*O*-octadecanoyl glycerol



15 1-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol



16 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-2-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol



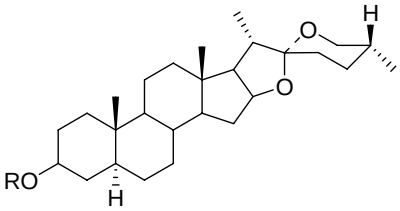
17 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*-(9*Z*-octadecenoyl) glycerol

Fig. 4 Structures of longchain glycerol

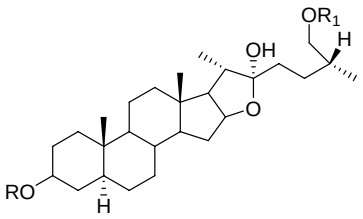
multiple gradient thin-layer chromatography (MGD-TLC) (Pobłocka, Matysik, and Cisowski, 2003).

HPLC was used to determine the content of three alkaloids, atropine, hyoscyamine, and scopolamine in the *H. niger* seeds (Wang, Pan, and Zhang, 2002; Ma, Chen, and Yang, 1996; Xing and Yin, 2006; Li *et al*, 1999). An orthogonal test was performed to optimize the processing technology. The results showed that *H. niger* seeds possessed the highest content of atropine sulfate and scopolamine hydrobromide (Wang *et al*, 2009), while soaked with vinegar for 2 h and dried with microwave for 4 min at low temperature in the rate of 40 kg of vinegar to 100 kg of the seeds. The content of total alkaloids in the seeds of *H. niger* was determined by ultraviolet spectrophotometry (Li *et al*, 1999; Li, Lu, and Li, 1995) and acid dye colorimetry respectively (Yang *et al*, 2009). At the same time, the seeds boiled with vinegar, the ones stir-fried with mixture of vinegar, and the stir-fried ones were also determined. The ones boiled with vinegar possessed the highest content of total alkaloids, followed by the ones stir-fried with mixture of vinegar, the raw medicinals, and the stir-fried ones in sequence.

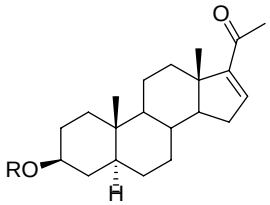
The composition and content of fatty acid in *H. niger* seed oil were analyzed by GC. Ten fatty acids such as oleic acid and linoleic acid were identified. The content of oleic acid is 16.32% and linoleic acid is 74.81% (Sun, 2000). The species of *Hyoscyamus* L. were characterised by high unsaturation ratio. Linoleic acid was the dominant fatty acid of the oil, which had bio-activities of lowering blood pressure and constriction of smooth muscle. *H. niger* seeds give considerable yield of



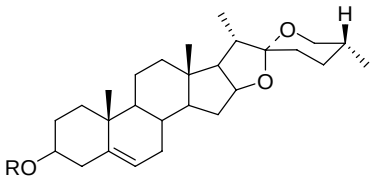
18 hyoscyamoside B R=Glc (1-3) Gal
19 hyoscyamoside C R=[Glc (1-3)] [Glc (1-2)] Gal
23 hyoscyamoside A R=Gal
24 hyoscyamoside B_1 R=Glc (1-4) Gal
25 hyoscyamoside B_2 R=Rha (1-2) Glc
27 hyoscyamoside C_1 R=Glc (1-2) Glc (1-4) Gal



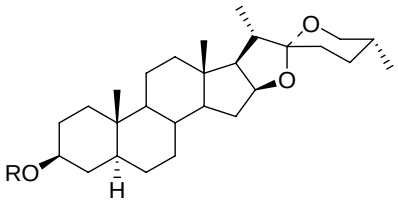
28 hyoscyamoside E R=Glc (1-4) Gal; R_1=Glc
29 hyoscyamoside F_1 R=Glc (1-2) Glc (1-4) Gal; R_1=Glc



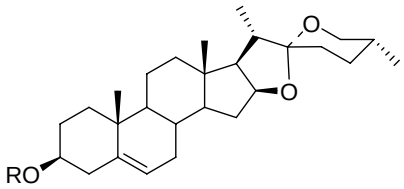
20 hyoscyamoside C_2 R=Glc (1-2) Glc (1-4) Gal



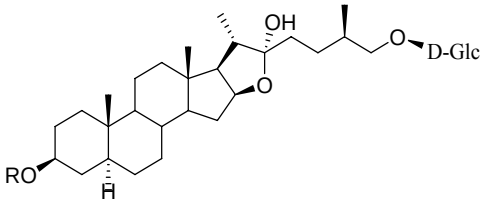
26 hyoscyamoside B_3 R=Rha (1-2) Glc



21 (25*R*)-5α-spirostan-3β-ol-3-*O*-β-*D*-glucopyranosyl-(1→3)-β-*D*-galactopyranoside R= β-*D*-Glc-(1→3)-β-*D*-Gal
22 (25*R*)-5α-spirostan-3β-ol-3-*O*-β-*D*-glucopyranosyl-(1→3)-[β-*D*-glucopyranosyl-(1→2)]-β-*D*-galacto-pyranoside R=β-*D*-Glc-(1→2)-β-*D*-Gal-β-*D*-Glc-(1→3)
30 atroposide A R=β-*D*-Gal
31 atroposide C R=β-*D*-Glc-(1→4)-β-*D*-Gal
32 (25*R*)-5α-spirostan-3β-ol-3-*O*-α-*L*-rhamnopyranosyl-(1→2)-β-*D*-glucopyranoside R=α-*L*-Rha-(1→2)-β-*D*-Glc
34 atroposide E R=β-*D*-Glc-(1→2)-β-*D*-Glc-(1→4)-β-*D*-Gal

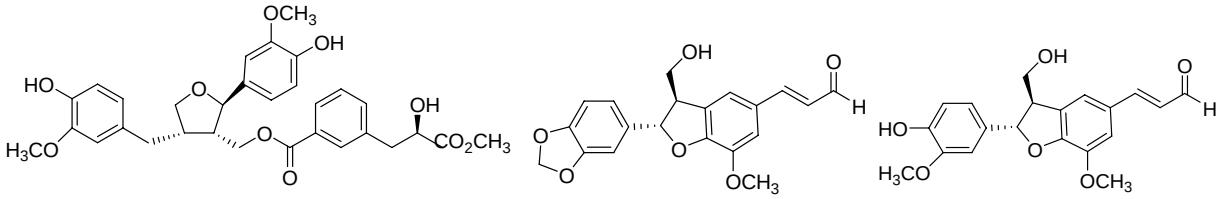


33 (25*R*)-spirost-5-ene-3β-ol-3-*O*-α-*L*-rhamnopyranosyl-(1→2)-β-*D*-glucopyranoside R=α-*L*-Rha-(1→2)-β-*D*-Glc



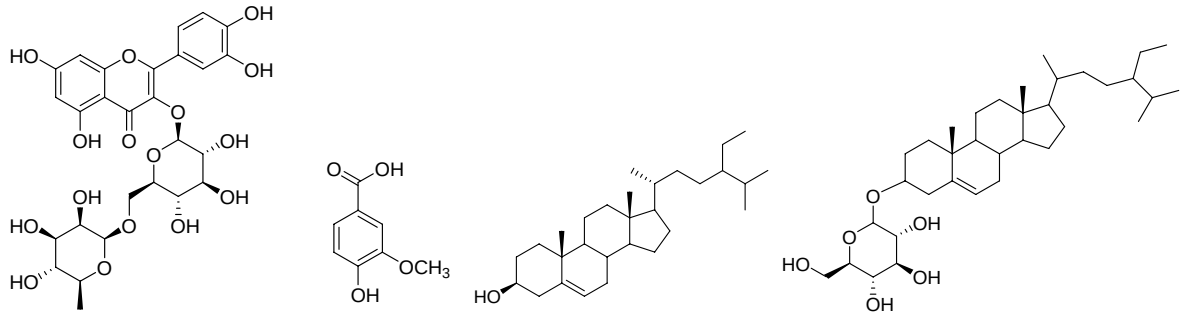
35 petunioside L R= β-*D*-Glc-(1→4)-β-*D*-Gal
36 pyranoside N R= β-*D*-Glc-(1→2)-β-*D*-Glc-(1→4)-β-*D*-Gal

Fig. 5 Structures of saponins and glycosides



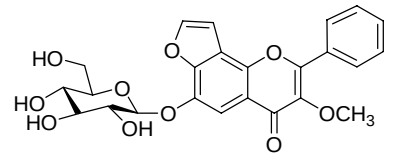
37 hyosmin **38** hyoscyamal **39** balanophonin

Fig. 6 Structures of lignans

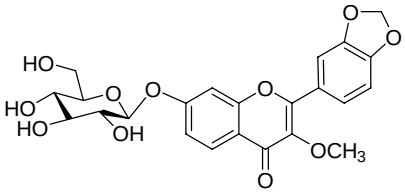


40 rutin **41** vanillic acid **42** β-sitosterol **43** daucosterol

Fig. 7 Structures of other compounds



48 pongamoside C



49 pongamoside D

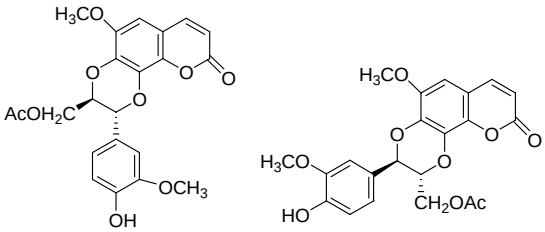
Fig. 8 Structures of flavonoidal glucosides

oil which seems to be a good source of essential fatty acids and lipid-soluble bioactive compounds. Tocopherols and sterols may be of medicinal importance at the level estimated (Ramadan, Zayed, and El-Shamy, 2007).

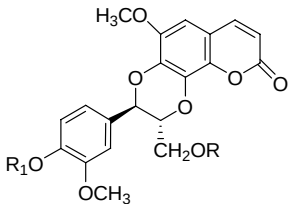
GC was developed to determine the content of 13 residues of organic chloride pesticides in *H. niger* seeds (Liu and Sui, 2007; Sui, 2006).

Pharmacological researches

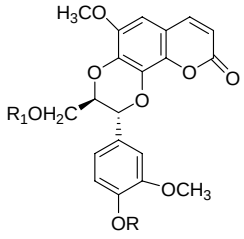
H. niger seeds are well documented in the traditional system of Chinese medicine for its effects of spasmolysis, analgesia, relieving cough, and anti- asthma, prescribed for the treatment of stomach cramps, heavy



50 hyosgerin **51** venkatasin



52 cleomiscosin A R=R_1=H
53 cleomiscosin B R=Ac; R_1=H
54 cleomiscosin A methyl ether R= H; R_1=Me



55 cleomiscosin A-9′-acetate; R=R_1=H
56 cleomiscosin B-9′-acetate; R=H; R_1= Ac

Fig. 9 Structures of coumarinolignans

coughs, neuralgia, and manic psychosis (Pharmacopoeia Committee of P. R. China, 2010). In Tibetan medicine, they are used as anthelmintic, antitumor, and febrifuge.

They are also found to be useful in the treatment of stomach/intestinal pain due to worm infestation, toothache, inflammation of the pulmonary region and tumors (Tsarong and Tsewang, 1994). Based on the above facts, a few of pharmacological experiments were performed to rationalize some of its medicinal uses.

Cardiovascular inhibitory effects

It was studied that the methanol extracts of *H. niger* seeds exhibited hypotensive, cardiodepressant and vasodilator effects, causing a dose-dependent (10－100 mg/kg) fall in the arterial blood pressure (BP) of rats under anesthesia. In guinea-pig atria, the extract exhibited a cardiodepressant effect on the rate and force of spontaneous atrial contractions. In isolated rabbit aorta, it (0.01－1.0 mg/mL) relaxed the phenylephrine (PE, 1 mmol) and K^+ (80 mmol) induced contractions and suppressed PE (1 mmol) control peaks obtained in Ca^{2+} free medium similar to that caused by verapamil. Its vasodilator effect was endothelium-independent as it was not opposed by N_ω-*N*-*L*-arginine methyl ester in endothelium-intact rat aortic preparations and also occurred at a similar concentration in endothelium-denuded tissues. These data indicated that *H. niger* lowered BP possibly through the inhibition of Ca^{2+} influx and its release (Khan and Gilani, 2008). Flavonoids have been shown to possess vasodilator effect through multiple mechanisms including Ca^{2+} channel blockade (Taggart *et al*, 1997; Ajay, Gilani, and Mustafa, 2003) and are considered protective against cardiovascular diseases such as hypertension and arrhythmias (Knekt *et al*, 1996; Pietta, 1998).

Cardiodoron, known as a modulating medicine in the treatment of functional disturbances of the cardiovascular system, is a composition of extracts of the blossoms from *Primula officinalis* L. and *Onopordon acanthium* L. and from the herbs of *H. niger*. Cardiodoron was used as a long term regulating treatment of heart failure, arrhythmia, and hypertension. With Cardiodoron, the mean heart rate at night (HRn) showed a tendency towards a normalization: in subjects with a low HRn the heart rate was increased and in subjects with a hight HRn the heart rate was decreased (Mariania *et al*, 2009; Cysarz *et al*, 2000).

Effects on central nervous system

Anxiolytic and sedative activity: *H. niger* leaves contain alkaloids, including scopolamine, which could relieve muscle tremors of central nervous system origin, inhibit central nervous system, and have a sedative effect (Jellin *et al*, 2000; Blumenthal *et al*, 1998).

Anticonvulsant activity: the methanolic extract of *H. niger* (300 mg/kg ip) significantly delayed the onset of seizures induced by picrotoxin (12 mg/kg ip) in mice, which certificated its anticonvulsant activity. Anti-seizure effect of *H. niger* may be partly related to the flavonoid, rutin in the extract (Ma, Lin, and Che, 2002). Animal experiments showed that flavonoids exerted their effects through the central benzodiazepine receptors (Reza *et al*, 2009).

Anti-inflammatory, analgesic, and antipyretic activities: the methanolic extract of *H. niger* seeds produced significant increase in hot-plate reaction time, while decreasing writhing response in a dose-dependent manner in mice indicated its analgesic activity. It has been assumed that both central and peripheral mechanisms are involved in the analgesic activity of the extract. It significantly inhibited carrageenin-induced paw edema and cotton pellet granuloma in rats. The extract in dose of 800 mg/kg also exhibited antipyretic activity in yeast-induced rat's pyrexia model. The bioactive extracts under chemical investigation showed that cleomiscosin A was an important constituent responsible for anti-inflammatory activity (Begum *et al*, 2010). Furthermore, the water decoction of *H. niger* seeds was also confirmed to have analgesic and anti-inflammatory function in mice (Wang *et al*, 2008).

Relaxant effects on smooth muscle

The crude extract of *H. niger* seeds caused a complete concentration-dependent relaxation of spontaneous contractions of rabbit jejunum inhibited partially by atropine. It also could inhibit contractions induced by carbachol (l μmol) and K^+ (80 mmol) in isolated rabbit jejunum, guinea-pig trachea, guinea-pig ileum, and rabbit urinary bladder tissues, which was similar to that of dicyclomine, but different from verapamil and atropine. The extract shifted the Ca^{2+} concentration-response curves to the right, similar to that caused by verapamil and dicyclomine, suggesting a Ca^{2+} channel-blocking mechanism in addition to an anticholinergic effect. In the guinea-pig ileum, it produced a rightward parallel shift of the acetylcholine curves, followed by a nonparallel shift with suppression of the maximum response at a higher concentration,

similar to that caused by dicyclomine, but different from that of verapamil and atropine. It exhibited antidiarrhoeal and antisecretory effects against castor oil induced diarrhoea and intestinal fluid accumulation in mice. In guinea-pig trachea and rabbit urinary bladder tissues, it caused relaxation of carbachol (1 μmol) and K^+ (80 mmol) induced contractions at around 10 and 25 times lower concentrations than in gut, respectively, and shifted carbachol curves to the right. Only the organic fractions of the extract had a Ca^{2+} antagonist effect, whereas both organic and aqueous fractions had anticholinergic effect. The alkaloids, including hyoscyamine and scopolamine, competitively inhibit acetylcholine, causing anti-cholinergic and parasympathetic effects. These results suggest that the antispasmodic effect of *H. niger* is mediated through a combination of anticholinergic and Ca^{2+} antagonist mechanisms. The relaxant effects of the extract occur at much lower concentrations in the trachea and bladder. This study offers explanations for the medicinal use of *H. niger* in treating gastrointestinal and respiratory disorders and bladder hyperactivity (Gilani *et al*, 2008). With storage, hyoscyamine converts to atropine. The inhibition of acetylcholine affects the muscarinic action but not the nicotinic effects of acetylcholine on ganglia and motor endplates. Henbane causes smooth muscle relaxation particularly in the gastrointestinal tract (Jellin *et al*, 2000).

Antitumor activity

The 11 compounds hyoscyamide, 1,24-tetracosanediol diferulate, 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*-nonadecanoyl glycerol, grossamide, cannabisin D, cannabisin G, *N*-*trans*-feruloyl tyramine, 1-*O*-octadecanoyl glycerol, 1-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol, 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-2-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol, and 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*-(9*Z*-octadecenoyl) glycerol were subjected to a screening test for cytotoxicity using human prostate cancer LNCaP cells. Grossamide, cannabisin G, and cannabisin D displayed low levels of inhibitory activity; Other compounds were inactive (Ma, Liu, and Che, 2002).

Feeding deterrent activity

Grossamide and cannabisin D have been shown to possess feeding deterrent properties (Lajide, Escoubas, and Mizutani, 1995).

Side effects and toxic reactions

In the ancient Chinese monographs, *H. niger* was recorded to have drastic toxicity. Since *H. niger* contains tropines alkaloids, it has a narrow range of use safety. Excessive doses can cause poisoning and death. But there is insufficient reliable information available about the safety of the topical use of henbane (Jellin *et al*, 2000). When the water extract of *H. niger* seeds was ig administered in mice to perform the acute toxicity experiment, none of the mice died due to intoxication (Wang *et al*, 2008).

The alkaloids like atropine, hyoscyamine, and scopolamine could cause permanent effect on brain development in inbred mice. They produce a typical antimuscarinic action by paralyzing the nerve endings of the parasympathetic system. The central anti-cholinergic syndrome is characterized by thought impairment, recent memory disturbance, hallucinations, hyperpyrexia, ataxia, excitement, drowsiness, coma, dry skin and flushing, tachycardia, mydriasis, and absence or reduction of bowel movements. The therapy including gastrointestinal decontamination, gastric lavage, supportive therapy, and physostigmine, is recommended if tachycardia, somnolence, coma, and threatens respiratory arrest are developed (Longo, 1966).

High doses can be toxic. It produces strong soporific effects and hallucinations (accompanied by the sensation of flight), which are typically accompanied by a number of side effects, disorientation, temporary memory loss, profuse sweating, and severe bodily discomforts (Prance and Nesbitt, 2005). *H. niger* intoxication includes the clinical signs of inappropriate speech, aggressiveness, nausea and vomiting, dilatation of pupils, flushing, somnolence, tachycardia, dizziness and ataxia, agitation, dryness of mouth, visual hallucinations, pyrexia, tremor and convulsion, dysphagia, distension of the bladder and abdomen, respiratory arrest, and coma, *etc*. And its therapy includes stomach lavage, supportive therapy, and physostigmine as a specific antidote (Doneray, Orbak, and Karakelleoglu, 2007). Administration of *H. niger* as anticholinergic agents in pregnancy could exert its permanent effect on brain development in inbred mice (Mahmoodi *et al*, 2004).

Discussion

For the chemical researches, besides the tropane

alkaloids in *H. niger*, non-alkaloids were isolated from this plant including some new structures. For the new structures, there is no report on their activities. We need more studies for these compounds in the aspects of pharmacological activities and mechanisms.

Nowadays in some Chinese patent medicines for treating cancers, *H. niger* seeds are used as the main ingredients. According to the above reports, some compounds have inhibitory effects on tumor cells growth. But pharmacological mechanism of the activity has not been studied clearly. We could get study both *in vivo* and *in vitro*, thus to provide more scientific basis for the clinical use of this medicinal plant and at the same time to extend the range of its clinical use.

It also has the activities of anti-inflammation and analgesis, *etc*, which is the basis of the functions of this plant. But the compounds responsible for these activities have not been elaborated clearly. So further studies both *in vivo* and *in vitro* should be taken into consideration.

Since the ancient time, the tropane alkaloids have been considered as the main constituents in *H. niger*. They are the active constituents with toxicity in this plant. The control of the toxicity is very important for the clinic safety. But there was no detailed study on the toxic mechanism for this medicinal plant. In this aspect, we need further study to elaborate the toxicity and its acting mechanism. And also the limits of the toxic constituents should be stipulated according to more scientific basis.

Currently, based on *Chinese Pharmacopoeia*, atropine sulfate and scopolamine hydrobromide are taken as the index compounds to control the quality of the medicinal herb. But these two compounds have no specificity to *H. niger*. Besides them, we need consider some other testing index with good specificity and/or activity to this medicinal plant. Based on more chemical and pharmacological studies, the theoretical basis could be provided to find some new index compounds to control the quality of this medicinal herb. Thus the quality standard could be improved more scientifically and effectively.

In conclusion, the survey of the chemical and pharmacological researches in *H. niger* was summarized, which could be of medicinal importance for the R & D of this medicinal herb.

References

Ajay M, Gilani AH, Mustafa MR, 2003. Effects of flavonoids on vascular smooth muscle of the isolated rat thoracic aorta. *Life Sci* 74(5): 603-612.

Begum AS, Verma S, Sahai M, Asai T, Hara N, Fujimoto Y, 2006. Hyosmin, a new lignan from *Hyoscyamus niger* L. *J Chem Res* 8: 675-677.

Begum AS, Verma S, Sahai M, Schneider K, Süssmuth R, 2009. Hyoscyamal, a new tetrahydrofurano lignan from *Hyoscyamus niger* Linn. *Nat Prod Res* 23(7): 595-600.

Begum S, Saxena B, Goyal M, Ranjan R, Joshi VB, Rao CV, Krishnamurthy S, Sahai M, 2010. Study of anti-inflammatory, analgesic and antipyretic activities of seeds of *Hyoscyamus niger* and isolation of a new coumarinolignan. *Fitoterapia* 81(3): 178-184.

Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Klein S, Riggins CW, Rister RS, 1998. *The Complete German commission E monographs*. American Botanical Council. Austin, 146.

British Herbal Medicine Association, 1996. *British Herbal Pharmacopoeia*. Biddles: London, 109.

British Pharmacopoeica Commission, 2010. *British Pharmacopoeia* (Vol 3). The Stationery Office: London, 3786.

Cysarz D, Schürholz T, Bettermann H, Kümmell HC, 2000. Evaluation of modulations in heart rate variability caused by a composition of herbal extracts. *Drug Res* 50(5): 420-424.

Doneray H, Orbak Z, Karakelleoglu C, 2007. Clinical outcomes in children with *Hyoscyamus niger* intoxication no receiving physostigmine therapy. *Eur J Emergency Med* 14(6): 348-350.

Gilani AH, Khan AU, Raoof M, Ghayur MN, Siddiqui BS, Vohra W, Begum S, 2008. Gastrointestinal, selective airways and urinary bladder relaxant effects of *Hyoscyamus niger* are mediated through dual blockade of muscarinic receptors and Ca^{2+} channels. *Fundam Clin Pharmacol* 22: 87-99.

Gruenwald J, Brendler T, Jaenicke C, 2004. *PDR for Herbal Medicines* (3rd ed). Montvale, Thomson PDR: USA, 431.

Jellin JM, Gregory P, Batz F, Hitchens K, 2000. Pharmacist's Letter/Prescriber's Letter Natural Medicines Comprehensive Database (3rd ed). Stockton, CA: Therapeutic Research Faculty.

Khan AU, Gilani AH, 2008. Cardiovascular inhibitory effects of *Hyoscyamus niger*. *Methods Find Exp Clin Pharmacol* 30(4): 295-300.

Knekt P, Jarvinen R, Reunanen A, Maatela J, 1996. Flavonoid intake and coronary mortality in Finland: A comparative study. *Br Med J* 312(7029): 478-481.

Lajide L, Escoubas P, Mizutani J, 1995. Termite antifeedant activity in *Xylopia aethiopica*. *Phytochemistry* 40(4): 1105-1112.

Li HF, Lu JX, Li W, 1995. Analysis of total alkaloids in the seeds of *Hyoscyamus niger* in five different habitats. *Chin J Pharm Anal* 15(S): 418-419.

Li HF, Lu JX, Zhang XM, Dong ZH, 1999. Analysis of total alkaloids in the seeds of *Hyoscyamus niger* in five different habitats. *Chin Tradit Herb Drugs* 30(8): 582-583.

Li HF, Zhang QW, Zhang XM, Dong WL, 1999. Determination of 3 alkaloids in the seeds of *Hyoscyamus niger* by ion pair chromatography. *Chin Tradit Herb Drugs* 30(3): 184-185.

Liu SY, Sui WB, 2007. Study on residues of organic chloride pesticides in Chinese medicinal materia. *J Inner Mongolia*

Normal Univ: *Nat Sci Ed* 36(1): 91-93.

Longo VG, 1966. Behavioral and electroencephalographic effects of atropine and related compounds. *Pharmacol Rev* 18: 965-996.

Lunga I, Bassarello C, Kintia P, Shvets S, Piacente S, Pizza C, 2008a. Steroidal glycosides from the seeds of *Hyoscyamus niger* L. *Nat Prod Communications* 3(5): 731-734.

Lunga I, Kintia P, Shvets S, Bassarello C, Piacente S, Pizza C, 2008b. Steroidal saponins from the seeds of *Hyoscyamus niger* L. *Chem J Moldova. Gen Industrial Ecol Chem* 3(1): 89-93.

Ma CY, Chen DC, Yang ZQ, 1996. Determination of alkaloids in *Hyoscyamus niger* by reverse phase ion-pair HPLC as well as TLC identification of *Hygrophila niger* and *H. megalantha*. *Chin J Pharm Anal* 16(2): 119-122.

Ma CY, Liu WK, Che CT, 2002. Lignanamides and nonalkaloidal components of *Hyoscyamus niger* seeds. *J Nat Prod* 65: 206-209.

Ma CY, Williams ID, Che CT, 1999. Withanolides from *Hyoscyamus niger* seeds. *J Nat Prod* 62: 1445-1447.

Mahmoodi M, Parivar1 K, Roostaeean AH, Rohani AH, 2004. Effect of prenatal administration of *Hyoscyamus niger*, atropine and hyoscine on passive avoidance learning of inbred balb/c mice. *Int J Psychophysiology* 54: 191.

Mariania E, Donarinia C, Grampellaa D, Guerrerioa T, Landonia G, Portalupi E, 2009. Integrated treatment of cardiovascular common pathologies with conventional pharmacological therapy integrated with a typical remedy of anthroposophic medicine, Cardiodoron (Onopordon/Primula comp). *Eur J Integr Med* 1: 223-260.

Nanjing University of Traditional Chinese Medicine, 2006. *Dictionary of Chinese Materia Medica*. Book 1. Shanghai Scientific and Technical Publishers: Shanghai, 322.

Pharmacopoeia Committee of P. R. China, 2010. *Pharmacopoeia of People's Republic of China*. China Medical Science and Technology Press: Beijing.

Pietta P, 1998. *Flavonoids in Medicinal Plants*. In: Flavonoids in Health and Disease. Rive-Evans CV and Packer L (Eds.). New York: Marcel Dekker, 61-110.

Pobłocka L, Matysik G, Cisowski W, 2003. Multiple gradient TLC and densitometric analysis of *p*-coumaric acid in some medicinal plants from the family Solanaceae. *J Planar Chromatogr* 16: 76-79.

Prance GT, Nesbitt M, 2005. *The Cultural History of Plants*. Taylor and Francis Routledge: New York, 194.

Ramadan MF, Zayed R, El-Shamy H, 2007. Screening of bioactive lipids and radical scavenging potential of some Solanaceae plants. *Food Chem* 103: 885-890.

Reza HM, Mohammad H, Golnaz E, Gholamreza S, 2009. Effect of methanolic extract of *Hyoscymus niger* L. on the seizure induced by picritoxin in mice. *Pak J Pharm Sci* 22(3): 308-312.

Sajeli B, Sahai M, Süssmuth R, Asai T, Hara N, Fujimoto Y, 2006. Hyosgerin, a new optically active coumarinolignan, from the seeds of *Hyoscyamus niger*. *Chem Pharm Bull* 54(4): 538-541.

Spinella M, 2001. *The Psychopharmacology of Herbal Medicine: Plant Drugs That Alter Mind*, *Brain*, *and Behavior*. Mass. MIT Press: Cambridge, 375.

Steinegger E, Sonanini D, 1960. Flavones of *Hyoscyamus niger*. *Pharmazie* 15: 643-644.

Sui WB, 2006. Determination of residues of organic chloride pesticides in Chinese medicinal material. *Chem Anal Meterage* 15(3): 25-27.

Sun G, 2000. Study on the composition of fatty acid in *Hyoscyamus niger* seed oil. *Qinghai Sci Technol* 7(1): 24-25.

Taggart MJ, Menice CB, Morgan KG, Wray S, 1997. Effects of metabolic inhibition on intracellular Ca^{2+}, phosphorylation of myosin regulatory light chain and force in rat smooth muscle. *J Physiol* 499(2): 485-496.

Tsarong J, Tsewang, 1994. *Tibetan Medicinal Plants*. Tibetan Medical Publications: India.

Wang H, Pan L, Zhang XF, 2002. Quantitative analysis of three kinds of tropane alkaloids in *Hyoscyamus niger* L. and *Przewalskia tangutica* M axim. by HPLC. *Northwest Pharm J* 17 (1): 9-10.

Wang Y, Bai ZL, Li J, Chen JP, Jia TZ, 2008. Researches in acute toxicity, anti-inflammatory and analgesic effect of seeds of *Hyoscyamus niger*. *Chin-Med Mag China* 6(2): 5-7.

Wang Y, Bai ZL, Li J, Chen JP, Jia TZ, 2009. Optimation of processing technology for the seeds of *Hyoscyamus niger* with orthogonal experiment. *Chin Tradit Pat Med* 31(7): 1070-1072.

Xing GJ, Yin SH, 2006. Content determination of hyoscyamine and scopolamine in the seeds of *Hyoscyamus niger* by HPLC. *Chin Hasp Pharm J* 26(2): 236-237.

Yang D, Li J, Xie SQ, Men QM, Xiong Y, 2009. Contents determination of total alkaloids in seeds of *Hyoscyamus niger* and their processed samples by acid dye colorimetry. *Chin J Med Guide* 11(3): 481-482.