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Chemical constituents of *Picrorhiza* genus: a review

Jit Narayan Sah, Vinay Kumar Varshney

ABSTRACT

Picrorhiza (family Scrophulariaceae) is a small genus of two important endangered medicinal plant species- *Picrorhiza kurrooa* Royle ex Benth and *Picrorhiza scrophulariiflora* Pennel of the Indo-China Himalayan region. These species contain several bioactive compounds that have therapeutic properties. They are medicinally revered herbs used extensively in traditional as well as modern medicinal systems of India, China, Tibet, Nepal and Sri Lanka for various immune-related diseases. *P. kurrooa* is predominant in the western Himalayas of Northern India, while *P. scrophulariiflora* is mainly found in the Himalayan regions of Sikkim, Nepal and Tibet. *P. kurrooa* is used for the treatment of liver disorder, gastrointestinal and urinary disorders, fever, asthma and jaundice and possess anti periodic, cholagogue, stomachic, laxative and antiasthmatic activities. The roots part of *P. scrophulariflora* is used in traditional Chinese medicine for the treatment of damp-heat dysentery, jaundice and steaming bone disorder. The genus has attracted great interest so much so that it has been the subject of numerous chemical and pharmacological investigations. The secondary metabolites reported in *P. kurrooa* and *P. scrophulariiflora* for the period from 1949-2013 are reviewed and compiled in this paper. One hundred thirty-two chemical constituents belonging to different class of compounds from roots, rhizomes, seeds, stem and leaves of these two *Picrorhiza* species are listed and their bioactivities are described in an effort to demonstrate the development in the phytochemistry and therapeutic applications of *Picrorhiza* genus.

Keywords: *Picrorhiza* genus, Scrophulariaceae, chemical constituents.

1. Introduction

The genus *Picrorhiza* belongs to the family Scrophulariaceae and is an important medicinal plant comprised of two species, *Picrorhiza kurrooa* Royle ex Benth and *Picrorhiza scrophulariiflora* Pennel, which are extensively used in traditional as well as modern medicinal system in India, China, Tibet, Nepal and Sri Lanka for the treatment of various immune-related diseases[1-3]. The variability of major phyto-constituents within the same species at different altitudinal ranges indicate a significant relationship between the quality and quantity of active principles and the environmental factors such as different habitat and stress conditions of different geographical locations. *P. kurrooa* is used for the treatment of liver disorders, fever, asthma and jaundice[4-6], gastrointestinal and urinary disorders, leukoderma, snake bite, scorpion sting and inflammatory[7-10], hepatoprotective[11-13,10], anti-inflammatory[14-15], immunomodulatory[16], free radical scavenging[17], gastric ulcer [18, 19], anti-allergic and anti-anaphylactic activities[20], anti-hepatitis-B surface antigen activity[21]. *P. scrophulariiflora* is used as antidiabetic, antiasthmatic, cardioprotective, anti healing, antioxidant and antiradical activities[22], antiulcer[23] and anticancer activity[24], a selective enhancer of neuron growth[25]. *P. kurrooa* is reported for its immunomodulatory activity as an alternative adjuvant for vaccines[26] and *in-vitro* scavengers of oxygen free radicals and choleretic activity [27, 17]. The underground parts of *P. kurrooa* have been found to yield a crystalline product "Kutkin" or "Picroliv", which usually is a mixture of two major C9-iridoid glycosides, i.e. Picroside-I (6-*O*-trans cinnamoylcatalpol) and "Kutkoside" (10-*O*-vanilloylcatalpol) in the ratio of 1:1.5[11]. Kutkin is a mixture of picroside-I and picroside-II. *P. kurroa* has iridoid glycosides belongs to an important class of compounds due to their structural link between terpenoides and indole alkaloids therefore possessing spectrum of biological activities [28-31].

2. About *Picrorhiza* genus*:*

P. kurrooa Royle ex Benth and *P. scrophulariiflora* Pennell (Family: Scrophulariaceae), commonly known as kutki, is a threatened, small perennial medicinal herb of alpine region. The plant grows in Himalayan region in moist, rocky slopes as well as in organic soils. It is found in Himalayan region (Garhwal to Bhutan), southeast Tibet, north Burma and west China. It prefers to grow generally on the rocky crevices. It grows mostly on sloppy and cliffy mountains. It is distributed abundantly in Alpine Himalayas between 3000 to 5000 m[32]. It also found in the eastern and central regions but abundantly in the north western region growing on open, stony and grassy slopes and on the turf of glacial flats[33]. This is the first review on phyto-chemical examinations of *Picrorhiza* genus, which is very important for drug industries, biological and pharmacological activities and this would be highly useful for researchers.

3. Chemistry of *Picrorhiza* genus:

The chemistry of *Picrorhiza* genus has been widely studied and phyto-chemical examinations have led to characterization of 132 constituents from the different parts of plants such as rhizomes, roots, leaf, stem and seeds of *Picrorhiza* species. The chemical study on the *P. kurrooa* rhizomes shows the presence of iridoids[34], acetophenones[35] and cucurbitacins[36-38]. It is known to be rich source of picroside-I and II as major bioactive compounds[39, 40,7, 41]. *P. kurrooa* also contains pikuroside, veronicoside, phenol glycosides, a number of cucurbitacin glycosides and 4-hydroxyl-3-methoxy-acetophenone[42,43], whereas *P. scrophulariiflora* contains cyclopentanoid monoterpenes, caffeoyl glycosides, phenylethanoid glycoside and plantamajoside[44-46].The compounds are listed in Table 1.

4. Biological activities

A wide range of biological activities have been attributed to iridoids, such as antihepatotoxic, choleretic, hypolipidemic, anti-inflammatory, antispasmodic, antitumor, antiviral, purgative, immunomodulatory, antioxidant, anti-phosphodiesterase, neuritogenic, antidiabetic, antiasthmatic, cardioprotective, molluscicidal and leishmanicidal activities [47,22,48,49]. Similarly, the hepatoregenerative and hypolipidemic effects of Picroliv, the preparation was shown to have similar or more potent activities than silymarin, a purified fraction of *Silybum marianum* (Asteraceae*),* commonly used in the treatment of liver disorders[11]. Aucubin was also shown to potently inhibit phorbol ester-induced oedema in mice ears, while catalpol and picroside II were not active. The latter iridoids showed only minor anti-inflammatory effects upon topical administration[50]. Moderate anti-inflammatory activity of picroside-II when administered topically was confirmed later, while pikuroside was ineffective[41]. Picrosides II, III, V, 6-feruloylcatalpol, and minecoside moderately inhibited chemiluminescence generated by activated polymorphonuclear neutrophils (PMNs), while picroside I was not active; scavenging effects of these compounds were excluded[51]. Picroliv however, as well as picroside I, was shown to be moderate superoxide scavengers, while kutkoside showed only weak activity[17]. Furthermore, Picroliv protected cells against hypoxia, enhanced the expression of VEGF and HIF-1, selectively inhibited protein tyrosine kinase activity, and reduced PKC[52]. Caffeoyl Glycoside (CG) stimulated cell proliferation of splenocytes and peritoneal macrophages, and enhanced the cytotoxicity of natural killer (NK) cells significantly[53].

The biological activities of *P. Kurrooa* can be described as rhizome- diuretic[54, 55]; roots-antibacterial and antimicrobial activity[56] and alcoholic extracts of the roots being active against *Micrococcus pyogenes* var. *aureus* and *Escherichia coli*, *Staphylococcus aureus* and *Salmonella typhi*. *P. kurrooa* has been shown to reduce mortality due to *Plasmodium berghei* (parasite) and hepatitis-B (virus) hepatotoxicity. The aqueous extract of the roots showed moderate activity against *Staphylococcus aureus* and *Staphtyphi* and marked inhibition against *E. coli*[57]. The antifungal potential of alcoholic extract of *P. kurrooa* was tested against the yeast *Candida albicans*. The extract of this plant and its major constituents exhibited significant activity against fungi[58].

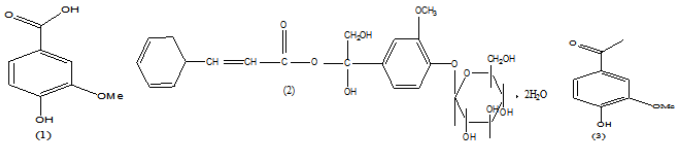
Picrorhiza species	Parts/ Extracts	Class of compounds	Chemical constituents (Constituent structure)	Ref.
P. kurrooa	Roots/ Pet. ether	Phenolic glycoside	vanillic acid: (4-Hydroxy-3-methoxy benzoic acid)**(1)**	39
		Iridoid glycoside	kutkin (**2**)	
		Phenolic glycoside	apocyanin (4'-hydroxy-3'-methoxy acetophenone) **(3)**	35
	Roots	Iridoid glycoside	picroside-I:[(2R,3S,4S,5R,6S)-6-[[(1aS, 1bS,2S,5a R,6S, 6aS)-6-hydroxy-1a-(hydroxymethyl)-2,5a,6,6a-tetrahydro-1bH-oxireno[5,6]cyclopenta [1,3-c]pyran-2-yl]oxy]-3,4,5-trihydroxyoxan-2-yl] methyl (E)-3 phenylprop-2-enoat **(4)**	40
			picroside-II**:** [1a-(hydroxymethyl)-2-[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-2,5a,6,6a-tetrahy dro-1bH-oxireno[5,6]cyclopenta[1,3-c]pyran-6-yl]4-hydroxy-3-methoxy benzoate (**5**)	7
			kutkoside : [1a,1b,2,5a,6,6a-Hexah ydro-6-hydroxy-1a-[[(4-hyd roxy-3-methoxy benzoyl)oxy] methyl]oxireno[4,5]cyclopeanta[1,2-c]pyran]-2-yl β-D-glucopyranoside (10 vanilloylcatalpol)(**6**)	59
			picroside-III: (1aS,1bS,2S,5aR,6S,6aS)-1a,1b,2,5a,6,6a-Hexahydro-6-hydroxy-1a-(hydroxymethyl)oxireno[4, 5]cyclopenta[1,2-c]pyran-2-yl beta-D-glucopyranoside 6- [(2E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate] **(7)**	60
	Roots/ MeOH $CHCl_3$	Cucurbitacin	25-Acetoxy-2-β-glucosyloxy-3,16,20-trihydroxy-9-methyl-18-norlanost-5,23-dien-22-one (**8**)	61

	Roots/EtOAc	Iridoid glycoside	picroside -V(6- m-Methoxybenzoylcatalpol)**(9)**	51
			veronicoside (**10**)	36
			minecoside (**11**)	
		Phenolic glycoside	picein (**12**)	
		Iridoid glycoside	6-feruloylcatalpol **(13)**	
		Phenolic glycoside	androsin**:** glucoacetovanillone; 4-acetyl-2-methoxyphenyl β-D-glucopyranoside; 3'-Meth oxy-4'-(β-D-glucopyranosyloxy) acetophenone (**14**)	
	Roots/ EtOAc	Cucurbitacins glycoside	25-acetoxy-2-β-glucosyloxy-16,20-dihydroxy-9-methyl-19-norlanosta-5,23-diene-3,11,22-trione (2-O-glycolside of cucurbitacin B) (**15**)	37
			25-acetoxy-2-β-glucosyloxy-16, 20-dihydroxy-9- methyl-19-norlanost-5-ene-3,11,22-trione (2-0-glucoside of 23, 24 dihyro cucurbitacin B) (**16**)	
			2-β-glucosyloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanosta-5, 23-diene-22-one (**17**)	
			2-β -glucosyloxy-3,16, 20,25-tetrahydroxy-9-methyl-19-norlanost-5-ene-22-one **(18)**	
			25-acetoxy-2- β-glucosyloxy -3,16, 20-trihydroxy-9-methyl-19-norlanosta-5,23-diene-11,22-dione (2-O-glucoside cucurbitacin) (**19**)	
			2-β-glucosyloxy-16,20-dihydroxy-9-methyl-19-norlanosta -5, 24-diene-3,11,22-trione (2-O-glucoside deacetoxy cucurbitacin B) (**20**)	
	Roots/ BuOH		arvenin III **(21)**	38
			2 β-glucosyloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanosta-5,23-diene -11,22-dione **(22)**	
			2- β-glucosyloxy-16,20,22-trihydroxy-9-methyl-19-norlanosta-5,24-diene-3,11dione(**23**)	
	Roots/ EtOAc		(23E)-25-acetoxy-2- β -D-glucosyloxy-3β-16α-dihydroxy-9β-methyl-19-nor-10α-lanosta-5,23-dien-22-one **(24)**	62
			(20R, 23Z)25-acetoxy-2-β -D-glucosyloxy-3β-,16α-20-tri hydroxyl-9β-methyl-19-nor-10α-lanosta-5, 23-dien-22-one (**25**)	
			2- β-D-glucosyloxy-3β,16α-dihydroxy-4,4,9β,14α-tetra methyl-19-nor-10α-pregn-5-en-20-one **(26)**	
			(20R)-25-acetoxy-2-β -D-glucosyloxy-3β-6α,20-trihydroxy- 9β-methyl-19-norlanost -5-en-22-one (**27**)	
			25-(acetyloxy)-2-(β-D-glucopyranosloxy)-3,16,-dihydr oxy-9-methyl-19-norlanosta-5,23-dien-22-one (**28**)	63
			25-(acetyloxy)-2-(β-D-glucopyranosyloxy)-3,16,20-trihydr oxy-9-methyl-19-nor lanosta-5, 23(Z)-dien-22-one **(29)**	
			25-(acetyloxy)-2-(β-D-glucopyranosyloxy)-3,16,20-trihy droxy-9-methyl-19-norlanost-5-en-22-one (**30**)	
			2-(β-D-glucopyranosyloxy)-3,16,20 trihydroxy-9-methyl-19-norlanosta-5, 24-dien-22-one (**31**)	
			2-(β-D-glucopyranosyloxy)-3,16-dihydroxy-4,4,9,14-tetra methyl-19-norpregn-5-en-20-one **(32)**	
			2,3,16,20,25-pentahydroxy-9-methyl-19-norlanost-5-en-22-one (**33**)	
			2-(6-O-cinnamoyl-β-D-glucopyranosyloxy)-3,16,20, 25 -tetrahydroxy-9-methyl-19-norlanost-5-en-22-on (**34**)	
	Roots/ MeOH		(2β,9β,10α,16 α,20ϵ,24 ϵ)-20, 24-epoxy-2-(β-D-glucopyranosyloxy)-16,25-dihydroxy-9-methyl-19-norl anost-5-ene-3,11-dione (**35**)	64
			2 β,3β,9β,10α,16α,20ϵ, 24ϵ)-20,24 epoxy-2-(β-D-glucopyranosyloxy)3,16,25-trihydroxy-9-methyl-19-norla nosta-5-ene-11-one (**36**)	
			(2β,9 β,10α,16α,20ϵ,24ϵ)-20,24-epoxy-2-(β -D-glucopyrano-syloxy)-16,25,26-trihydroxy-9-methyl-19-norlanost-5-en-3,11-dione (**37**)	
			(2β,3β,9β,10α,16α, 20ϵ,24ϵ)-20,24-epoxy-2-(β-D-glucopyranosyloxy)-3,16, 25, 26-tetrahydroxy-9-methyl-19-norlanost-5-en-11-one (**38**)	
			(2β,9β,10α,16α,20β,24Z)-2-(β-D-glucopyranosyloxy)-16,20,26-trihydroxy-9-methyl-19-norlanost-5,24-diene-3,11-dione (**39**)	
			(2 β,9β,10α,16α,20β,24Z)-2-(β-D-glucopyranosyloxy)-3,16,20, 26-tetrahydroxy-9-methyl-19-norlnost-5,24-diene-11-one (**40**)	
	Roots/ EtOAc	Iridoid glycoside	pikuroside: β-D-glucopyranoside, (3R,5S,5aS,6R,7S, 8R, 8aS)-hexahydro-8,8a-dihydroxy-7-[(4-hydroxy-3-methxy benzol) oxy]-3,6-methano-1H-cyclopenta[e] [1,3]dioxepin-5-yl **(41)**	41
	Seeds/ EtOAc		picrorhiza acid (1) (**42**)	65
			picrorhizoside A (2) (**43**)	
			picrorhizoside B (3) **(44)**	
			picrorhizoside C (4) **(45)**	
		Aliphatic homocyclic	(-)- shikimic acid (5) (**46**)	
		Phenolic glycoside	gallic acid (6) (**47**)	
			ellagic acid (7): 2,3,7,8-Tetrahydroxy-chromeno[5,4,3-cde] chromene-5,10-dione, (**48**)	
			isocorilagin (8) **(49)**	

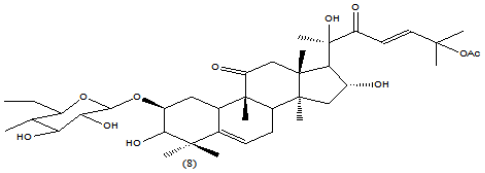
			1-O-galloyl-β-D-glucose (9) (**50**)	
			1-O,3-O,6-O-trigalloyl β-D-glucose (10) (**51**)	
			1-O,2-O,3-O,4-O,6-O-pentagalloyl-β-D-glucose (11) (**52**)	
			isochebulic acid **(12) (53)**	
	Seeds/ EtOAc	Triterpenoids	2α,3β,19β,23-tetrahydroxylean-12-en-28-O-β-D-glucoside **(54)**	66
			2α,3β,19β,23-tetra hydroxylolean-12-en-28-oic acid **(55)**	
			2α,3β,23-trihydroxyolean-12-en-28-O-β-D-glucoside (**56**)	
			2α,3β,19β, trihydroxyolean-12-en-28-oic acid **(57)**	
			2α,3β,19β-trihydroxyolean-12-en-28-oic acid (**58**)	
			2α,3β,6β-23-tetrahydroxyolean-12-en-28-oic acid(**59**)	
			2α,3β,23,2',3'4'6'-hepta-aetoxyl-19α-hydroxy-olean-12 -en-28-O-β-D-glucoside **(60)**	
			2α,3β,23-triacetoxyl -19α hydroxyl-olean-12-en-28-oic acid **(61)**	
P. scrophulariiflora	EtOH		picroside -I **(4)**	67
			picroside -II **(5)**	
			picroside -III**(7)**	
			vanillic acid**(1)**	
		Aliphatic homomonocyclic	cinnamic acid **(62)**E)-3-phenylprop-2-enoic acid	
			ferulic acid **(63)**	
	Roots/ n-BuoH	Cucurbitacin glycoside	2β-glucopyranosyloxy-3, 16,20,22-tetrahydroxy-9-methyl-19-norlanosta-5,24-diene**(64)**	68
			25- acetoxy-2β glucopayanosyloxy-3,16, 20-trihydroxy-9-methyl-19-norlansota-5,23diene-22-one**(8)**	
		Iridoid glycoside	amphicoside (picroside-**II**) **(5)**	
			catalpol **(65)**	
			acubin **(66)**	
		Phenolic glycoside	androsin **(14)**	
	Roots/ BuOH	Iridoid glycoside	picroside-IV: 6-[(2E)-3-(4-hydroxy phenyl)-2-propeno ate] (1aS,1bS,2S,5a R,6S,6aS)-1a,1b,2,5a,6,6a-hexah ydro-6-hydroxy-1a-(hydroxymethyl)oxireno [4,5] cyclopenta [1,2-c]pyran-2-yl β-D-glucopyranoside (**67**)	44
		Phenylethanoid glycoside	scroside A**:** 6-[(2E)-3-(3-hydroxy-4-methoxyphenyl) -2-propenoate]2-(3-hydroxy-4-methoxyphenyl)ethyl O-β-D-glucopyranosyl-(1→2)-O-β-D-glucpyranosyl-(1→3)-β-D-glucopyranoside **(68)**	
			scroside B: 6-[(2E)-3-(3-hydroxy-4-methoxyphenyl)-2-propenoate] 2-(3-hydroxy-4-methoxy phenyl)ethyl 3-O-β-D-glucopyranosyl-β-D-glucopyranoside **(69)**	
			scroside C: 4-[(2E)-3-(3-hydroxy-4-metho xyphenyl)-2-propenoate]2-(3-hydroxy-4-methoxyphenyl)ethyl O-β-D-glucopy ranosyl-(1→2)-O-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside **(70)**	
		Iridoid glycoside	specioside **(71)**	
			picroside -I **(4)**	
			picroside-II **(5)**	
			verminoside **(72)**	
			minecoside **(11)**	
			catalpol **(65)**	
			6-feruloylcatalpol **(13)**	
		Cucurbitacin glycoside	2-(β-D-glucopyranosyloxy)-3,16,20,25-tetrahydroxy-9-methyl-19-norlansota-5-ene -22-one**(18)**	
			2-(β-D-glucopyranosyloxy)-3,16,20-trihydroxy-9-methyl-19-norlansota-5,24-diene -22-one**(31)**	
		Phenylethanoid glycoside	plantamajoside **(73)**	
	Stems/ EtOAc /MeOH	Phenyl glycoside	scrophenoside A: (1-[4-(β-D-glucopyranosyloxy)-3-methoxyph enyl]ethanone 6-[4-(β-D-[glucopyranosyloxy)-3-methoxybenzoate](**74)**	69
			scrophenoside B : (1-[4-(β -D-glucopyranosyloxy)phenyl] ethanone 6-[(2E)-3-(4Hydroxy phenyl)prop-2-enoate] **(75)**	
			scrophenoside C: (4-(1-Hydroxyethyl)-2-methoxyphenyl -β-D-glucopyranoside**(76)**	
		Phenylethanoid glycoside	scroside D: (2-(3-Hydroxy-4-methoxyphenyl)ethyl 3-O-β-B-glucopyranosyl-β-D-glucopyranoside 4-[(2E)-3-(4-Hydroxy-3-methoxyphenyl)prop-2-enoate]**(77)**	
			scroside E: (2-(3-Hydroxy-4-methoxy phenyl)ethyl-3-O-β-D-Glucopyranosyl-β-D-glucopyranoside 6-[(2E)-3-(4-Hydroxy-3-methoxyphenyl)prop-2-enoate](**78)**	
			androsin**(14)**	
		Phenylpropanoid glycoside	hemiphroside : 2-(3-Hydroxy-4-methoxyphenyl) ethyl 3-O-β-D-Glucopyranosyl-β-D-glucopyranoside 4-[(2E)-3-(4-Hydroxy-3-methoxyphenyl)β-prop-2-enoate **(79)**	
		Pentacyclic triterpene	coniferin: (4-[(1E)-3-Hydroxyprop-1-enyl]-2-methoxy phenyl-β-D-Glucopyranoside **(80)**	
		Iridoid glycoside	6-O-cinnamoyl-D-glucopyranose **(81)**	
			6-O-(p-coumaroyl)-D-glucopyranose **(82)**	

	Roots	Phenyl ethyl glycoside	2-(3,4-dihydroxyphenyl)-ethyl-O-β-D-glucopyranoside **(83)**	70
			scroside D**(77)**	
			scroside B **(69)**	
			hemiphroside A **(79)**	
		Phenylethanoid glycoside	plantainoside D **(84)**	
			scroside A **(68)**	
			androsin **(14)**	
		Phenolic glycoside	piceoside (picein)**(12)**	
	Roots/EtOAc/n-BuOH	Cylopentene monoterpenes	piscrocin A **(85)**	45
			piscrocin B **(86)**	
			piscrocin C **(87)**	
	Rhizome/ n-BuOH	cucurbitacins	2-β-glucosyloxy-3,16,20,25-tetrahydroxy-9-methyl-19-norlanosta-5,23-diene-22-one (II) **(17)**	71
			picroside -I **(4)**	
			androsin **(14)**	
			scroside A **(68)**	
			scroside D **((77)**	
	Stems/ EtOAc/EtOH	Iridoid glycoside	piscroside A (1) **(88)**	72
			piscroside B (2) (**89)**	
			picroside -I **(4)**	
			picroside -II **(5)**	
			picroside -III **(7)**	
			picroside -IV **(67)**	
			6-O-trans-feruloylcatalpol**(90)**	
			minecoside **(11)**	
			verminoside **(72)**	
			catalposide : [(1aS,1bS,2S,5aR,6S,6aS)-1a-(hydroxy methyl)-2-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy -6- (hydroxylmethyl)oxan-2-yl]oxy-2,5a,6,6a-tetrahydro-1b H-oxireno[5,6]cyclopenta[1,3-c]pyran-6-yl]4-hydroxy benzoate**(91)**	
			aucubin **(66)**	
		Cucurbitacin glycoside	2β-glucopyranosyloxy-3,16,20,22-tetrahydroxy-9-methyl-19-norlanosta-5,24-diene**(64)** Wang et al 1993	
			2β-glucopyranosyloxy-3,16,20,22-tetrahydroxy-19-norlanosta-5,23-diene-22-ol **(17)**	
			25-aceloxy-2β-glucopyranosyloxy-3,16,20-trihydroxy-19-norlanosta-5,23-diene-22-ol **(19)**	
	Rhizomes/ n-BuOH	Non glycosidic iridoids	rehmaglutin A **(92)**	73
			rehmaglutin D (**93)**	
		Iridoid glycoside	3'-methoxyspecionin **(94)**	
			picroside -I **((5)**	
			picroside -II **(6)**	
			picroside -III (**7)**	
			pikuroside (IV) (**41)**	
	Stems	Phenylethanoid glycoside	scroside A **(68)**	74
			plantainoside D4 **(84)**	
			plantamajoside**(73)**	
	Roots/95% EtOH	Secoiridoids	picrosecoside -I **(95)**	75
			picrosecoside -II **(96**)	
	Rhizomes/ n-BuOH	Fatty acid	w-hydroxyhexadecanoic acid**(97)**	76
			apocynin **(3)**	
		Phenyl propenoid	syringaresinol 4-O-β-D-glucopyranoside **(98)**	
			vanillic acid **(1)**	
		Phenolic glycoside	Umbelliferon: 7- hydroxycoumarine**(99)**	
			cinnamic acid **(62)**	
		Aliphatic homomonocyclic	isoferulic acid : (E)-3-(3-hydroxy-4-methoxyphenyl) prop-2-enoic acid(**100)**	
			ferulic acid : (E)-3-(4-hydroxy-3-methoxyphenyl) prop-2-enoic acid(**63)**	
			picroside -II **(5)**	
			acubin **(71)**	
			scroside D **(77)**	
			coniferin (**80)**	
			minecoside **(14)**	
			catalpol **(66)**	
			Scroneoside-A: 1-(2 methoxy-4-actylphynyl) 6-O-[2E)-3-(3-methoxy-4-hydroxyphenyl)-propenoate]- β-D-glucopyranoside **(101)**	
		Phenylethanoid glycoside	scroside F: 1-[2-(3-hydroxy-4-methoxyphenyl)ethyl]-O-β-d-Glucopyranosyl-(1-2)-O- β-D-rhamnopyranosyl-(1-3)-6-O- [2E)-3-(3-methoxy-4-hydroxyphenyl)-propenoate]- β-D-glucopyranoside **(102)**	

	Roots/n-BuOH	Caffeoyl glucoside	1,6-di-O-caffeoyl-β-D-glucopyranoside (**103**)	77
	Roots/ n-BuOH	secoiridoids	picrogentioside A (1) **(104)**	78
			picrogentioside B (2) **(105)**	
			picrogentioside C (3) **(106)**	
			plantamajoside **(73)**	
			plantainoside **(84)**	
	Roots/n-BuOH	Caffeoyl glucoside	scrocaffeside A(1) **(107)**	46
			scrocaffeside A(2) (**108**)	
			scrocaffeside A (3) (**109**)	
			4-O-β-D-glucopyranosyl caffeic acid **(110)**	
			4-methoxycaffeic acid **(111)**	
			scroside D **(77)**	
	Roots/ 95% EtOH		11-O-galloylbergenin : (3,4,8,10-tetrahydroxy-9-methoxy-6-oxo-3,4,4a,10b-tetrahydro-2H-pyrano[3,2-c]isochromen-2-yl)methyl 3,4,5-trihydroxybenzoate (**112**)	79
		Phenolic glycoside	bergenin : (2R,3S,4S,4aR,10bS)-3,4,8,10-tetra hydroxy-2-(hydroxymethyl)-9-methoxy-3, 4,4a,10b-tetrahydro-2H-pyrano[3,2-c]isochromen-6-one (**113**)	
			arbutin : 4-hydroxyphenyl-β-D glucopyranoside **(114)**	
			androsin **(14)**	
		Pentacyclic triterpene	β-sitosterol : (3S,8S,9S,10R,13R,14S,17R)-17-[(2R,5R)-5-ethyl-6-methylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9, 11,12,14,15, 16,17-dodecahydro-1 H-cyclopenta[a]phenanthren-3-ol **(115)**	
		Sesquiterpene	daucosterol (lyoniside): (2R,3R,4S,5S,6R)-2-[[(3S,8S,9S,10R,13R,14S,17R)-17-[(2R,5R)-5-ethyl-6-methylheptan-2-yl]-10,13-dimethyl-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl]oxy]-6-(hydroxymethyl)oxane-3,4,5-triol**(116)**	
	Roots/95% EtOH	Alcoholic	hexacosanol **(117)**	80
		Phenolic glycoside	catechin : (2S,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol **(118)**	
			luteolin :2-(3,4-dihydroxyphenyl)-5,7-dihydro xychromen-4-one**(119)**	
		Phenyl propenoid	luteolin-7-O-β-D-glucoside **(120)**	
			gallic acid**(47)**	
			isoferulic acid: (E)-3-(3-hydroxy-4-methoxy phenyl)prop-2-enoic acid **(100)**	
			vanillic acid **(1)**	
		Phenylethanoid glycoside	scroside G **(121)**	
	Roots/EtOAc and BuOH		coniferin : 6-[(2E)-3-(4-hydroxyphenyl)-2-propeno ate] (1aS,1bS,2S,5a R,6S,6aS)-1a,1b,2,5a,6,6a-hexa hydro-6-hydroxy-1a-(hydroxymethyl)oxireno[4,5] cyclo penta [1,2-c]pyran-2-yl β-D-Glucopyranoside (**80**)	81
		Hydroquinone glycoside	arbutin**(114)**	
			androsin **(14)**	
	Stems		scrophuloside A (1S,4aS,6S,7S,7aS)-1-(β-D-glucopyranosyloxy)-6-{[(2E)-3-(4-methoxyphenyl)-2-propenoyl]oxy}-7-methyl-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-4-carboxylic acid**(122)**	82
			scrophuloside B2-(3,4-Dihydroxyphenyl)ethyl α-L-arabinopyranosyl-(1->6)-[6-deoxy-α-L-mannopyranosyl-(1->3)]-4-O-[(2Z)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoyl]-β-D-glucopyranoside**(123)**	
Neopicrorhiza scrophulariiflora	Roots/ BuOH	Non glycosidic iridoids	piscrocin D (**124**)	83
			piscrocin E (**125**)	
			piscrocin F (**126**)	
			piscrocin G (**127**)	
		Iridoid glycoside	piscroside A(8) **(88)**	
			piscroside B (9) **(89)**	
			rehmaglutin A **(95)**	
			rehmaglutin D **(96)**	
		Iridoid glycoside	(-)-3'- methoxyspecinonin **(128)**	
			pikuroside **(41)**	
			picroside -I **(4)**	
			picroside -II **(5)**	
			picroside -III**(7)**	
	Rhizomes/ EtOAc	Iridoid glycoside	picroroside A (**129**)	84
			picroroside B (**130**)	
			picroroside C (**131**)	
			picroside -I	
			picroside -II	
		Cucurbitacin glycoside	scrophoside A (**132**)	
			cucurbitacin **(28)**	
			cucurbitacin**(30)**	
			cucurbitacin **(31**)	



(1) (2) (3)



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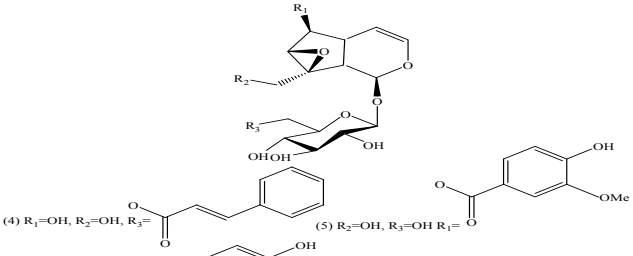
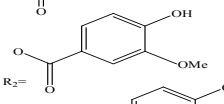
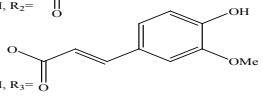


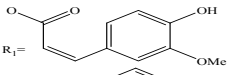
(4) R_1=OH, R_2=OH, R_3= (5) R_2=OH, R_3=OH R_1=



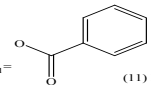
(6) R_1=OH, R_3=OH, R_2=



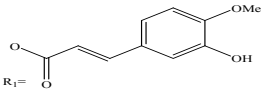
(7) R_1=OH, R_2=OH, R_3=



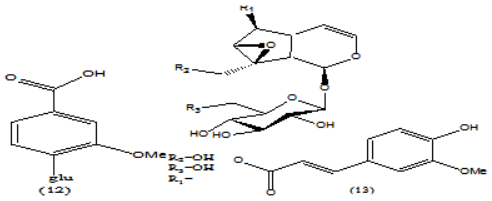
(9) R_2=OH, R_3=OH, R_1=



(10) R_2=OH, R_3=OH, R_1=



(11) R_2=OH, R_3=OH, R_1=



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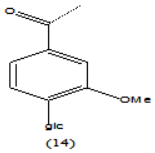

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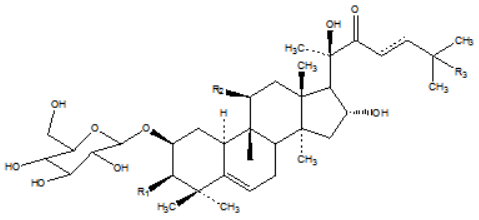
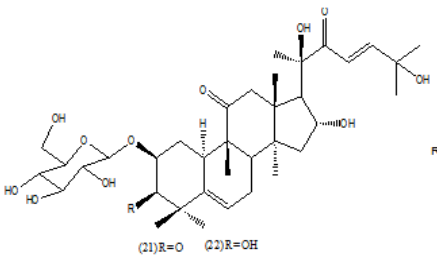
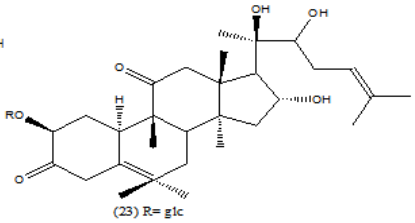


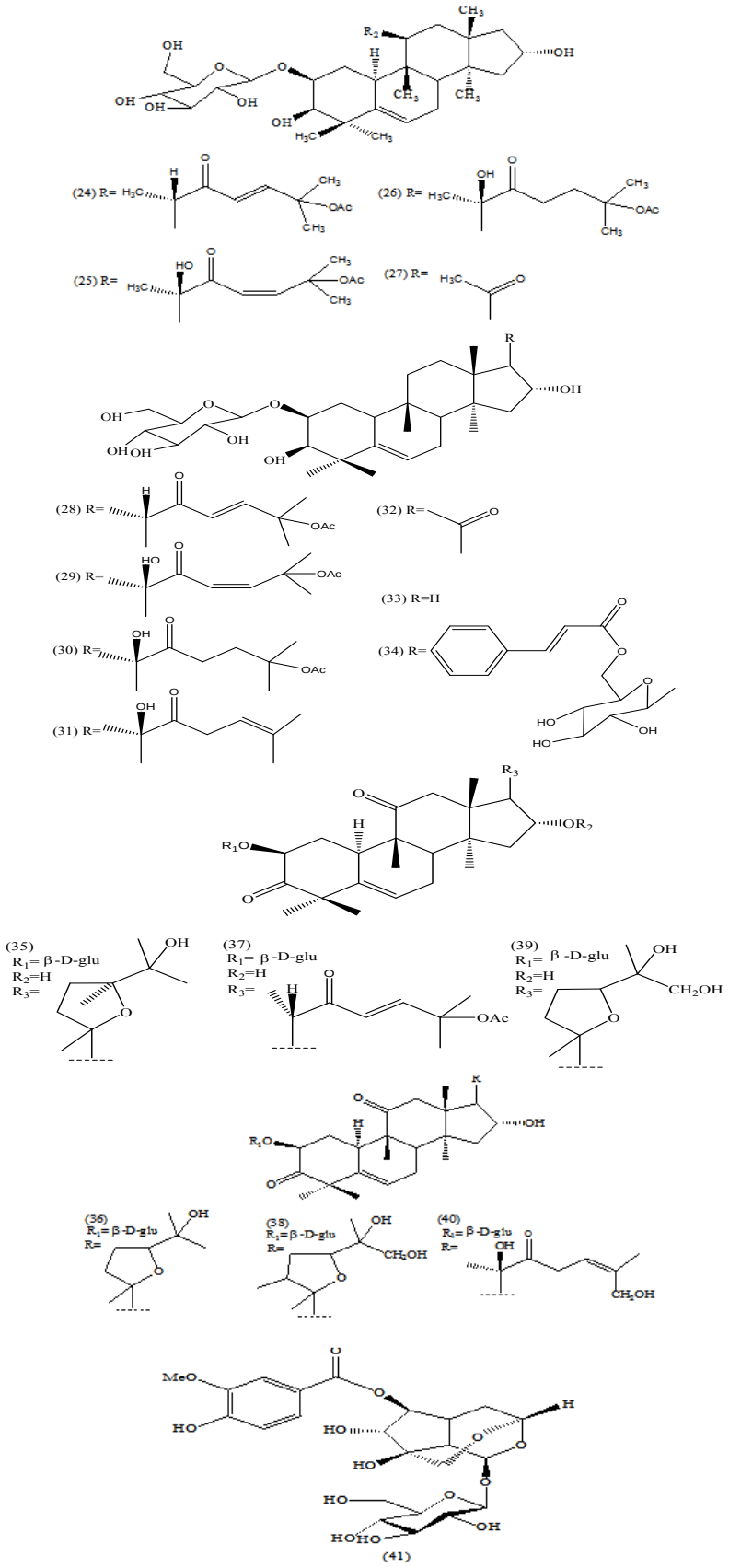
(15) R_1=O, R_2=O, R_3=OAc
(16) R_1=O, R_2=O, R_3= OAc
(17) R_1=HO, R_2=H2, R_3= OAc
(18) R_1=HO, R_2=H_2, R_3=OAc
(19) R_1=HO, R2=H_2, R_3=OH
(20) R_1=HO, R_2=O, R_3=OAc

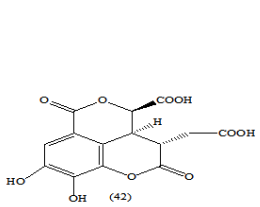


(21)R=O (22)R=OH



(23) R= glc


(24) R=
(26) R=
(25) R=
(27) R=
(28) R=
(32) R=
(29) R=
(33) R=H
(30) R=
(34) R=
(31) R=
(35)
R1= β -D-glu
R2=H
R3=
(37)
R1= β -D-glu
R2=H
R3=
(39)
R1= β -D-glu
R2=H
R3=
(36)
R1= β -D-glu
R=
(38)
R1= β -D-glu
R=
(40)
R1= β -D-glu
R=
(41)



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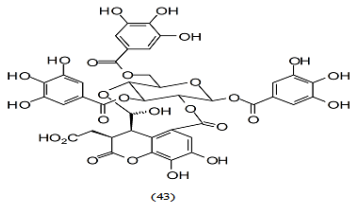

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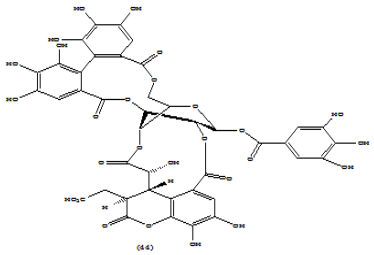

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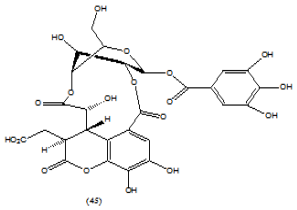

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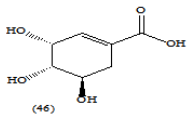

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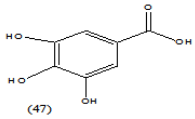

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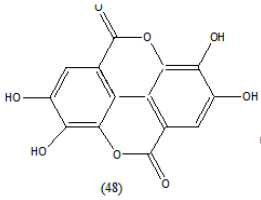

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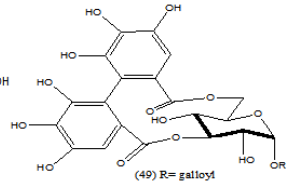
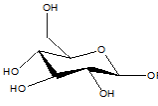
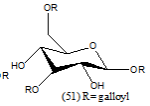


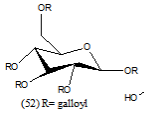
(49) R= galloyl



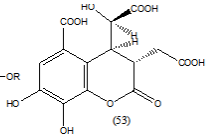
(50) R= galloyl



(51) R= galloyl



(52) R= galloyl



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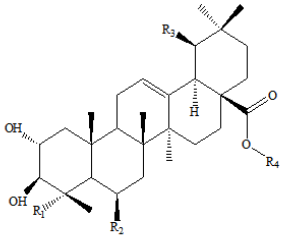
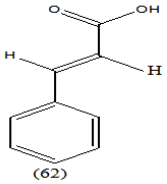


(54) R_1=CH_2OH, R_2=H, R_3=OH, R_4=glu
(56) R_1=CH_2OH, R_2=H, R3=OH R_4=glu
(58) R_1=CH_3, R_2=H, R_3=OH R_4=H
(60) R_1=OAc, R_2=H, R_3=OH, R_4=OH

(55) R_1=CH_2OH, R_2=H, R_3=OH R_4=H
(57) R=CH_2, R_2=H, R_3=H, R_4=H
(59) R_1=CH_2OH, R_2=OH, R_3=H, R_4=H
(61) R_1=OAc, R_2=OAc, R_3=OH, R_4=glu



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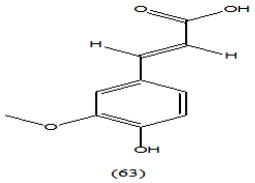

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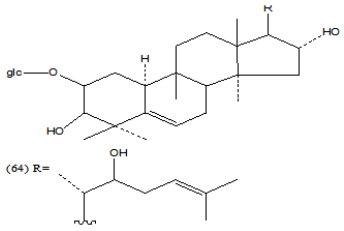
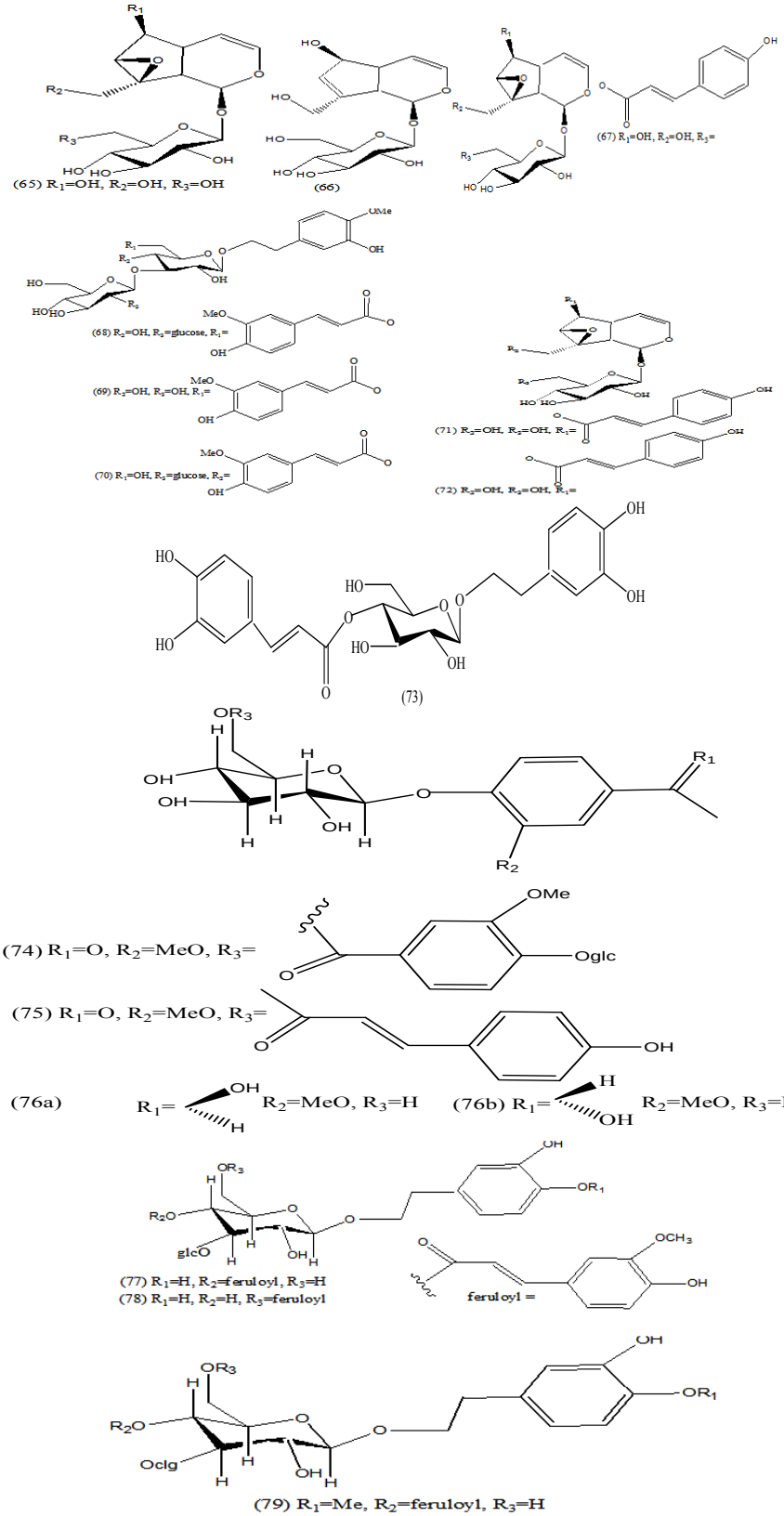
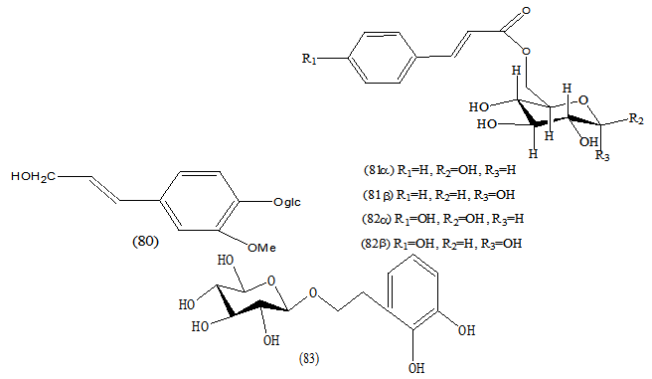
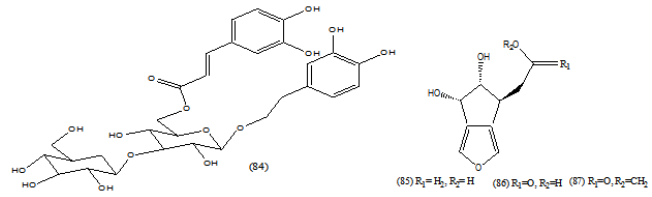
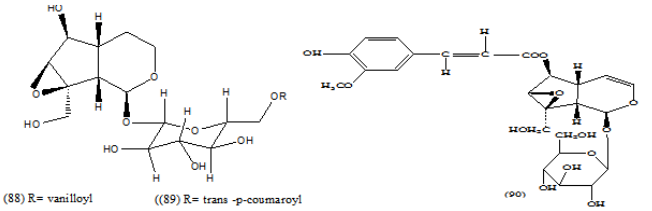


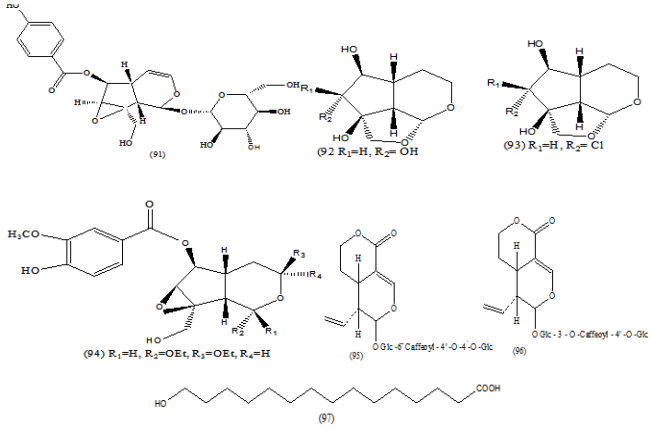
(64) R=

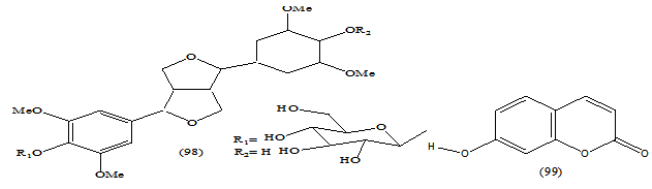

(65) R1=OH, R2=OH, R3=OH
(66)
(67) R1=OH, R2=OH, R3=
(68) R2=OH, R3=glucose, R1=
(69) R2=OH, R3=OH, R1=
(70) R1=OH, R2=glucose, R3=
(71) R2=OH, R3=OH, R1=
(72) R2=OH, R3=OH, R1=
(73)
(74) R1=O, R2=MeO, R3=
(75) R1=O, R2=MeO, R3=
(76a) R1= R2=MeO, R3=H
(76b) R1= R2=MeO, R3=H
(77) R1=H, R2=feruloyl, R3=H
(78) R1=H, R2=H, R3=feruloyl
feruloyl =
(79) R1=Me, R2=feruloyl, R3=H

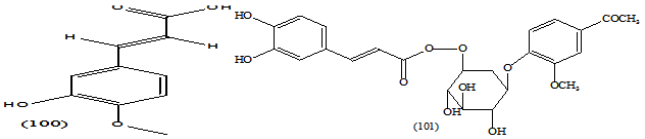

(80)
(81α) R1=H, R2=OH, R3=H
(81β) R1=H, R2=H, R3=OH
(82α) R1=OH, R2=OH, R3=H
(82β) R1=OH, R2=H, R3=OH
(83)

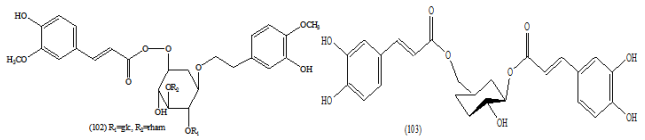

(84)
(85) R1= H2, R2= H
(86) R1=O, R2=H
(87) R1=O, R2=CH2

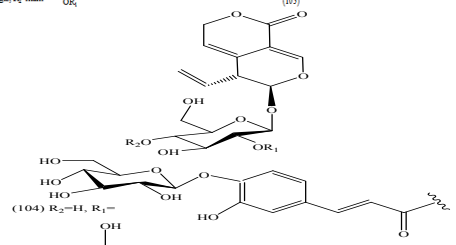

(88) R= vanilloyl
((89) R= trans -p-coumaroyl
(90)

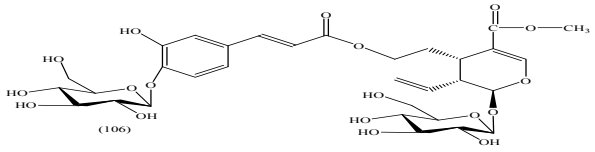

(91)
(92 R1=H, R2= OH
(93) R1=H, R2= Cl
(94) R1=H, R2=OEt, R3=OEt, R4=H
(95)
O Glc -6' Caffeoyl - 4' -O -4 -O -Glc
(96)
O Glc - 3 - O -Caffeoyl - 4' -O -Glc
(97)

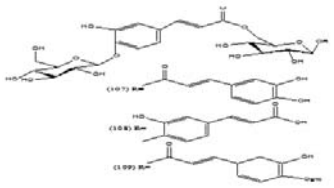

(98)
R1= HO
R2= H HO
(99)

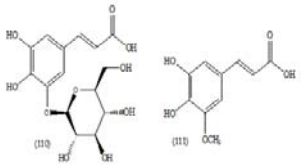

(100)
(101)

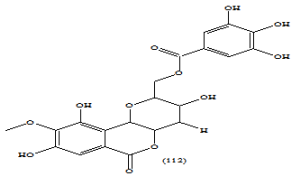

(102) R2=glc, R1=rham
(103)

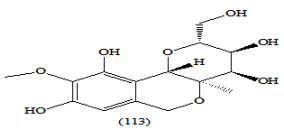

(104) R2=H, R1=
(105) R1=H, R2=


(106)




(110)
(111)


(112)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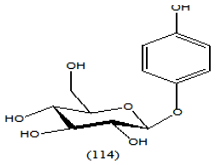
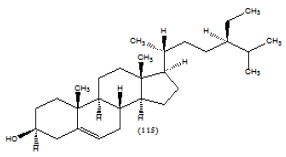

(114)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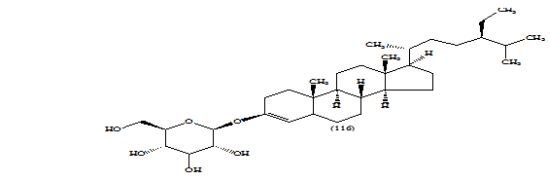
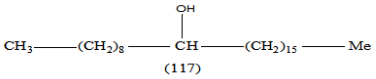
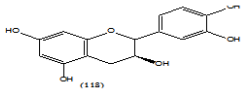


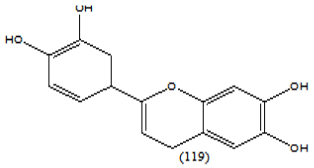
(116)



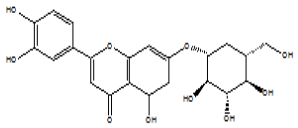
(117)



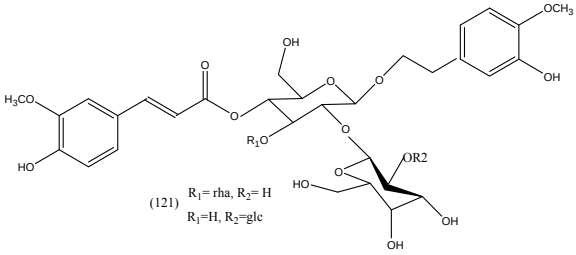
(118)



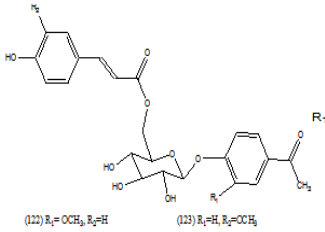
(119)



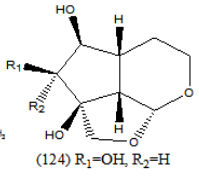
(120)



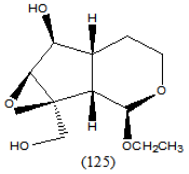
(121) R_1= rha, R_2= H
R_1=H, R_2=glc



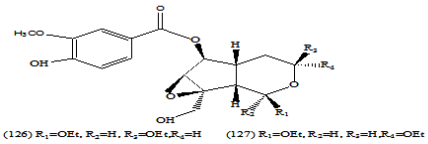
(122) R_1=OCH_3, R_2=H (123) R_1=H, R_2=OCH_3



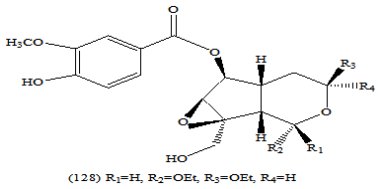
(124) R_1=OH, R_2=H



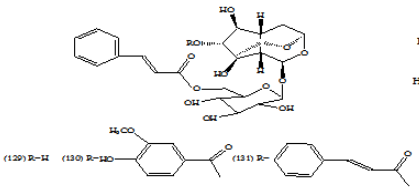
(125)



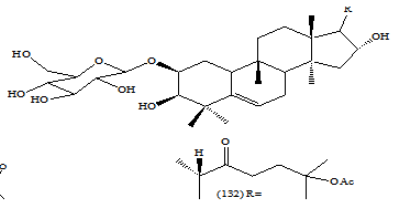
(126) R_1=OEt, R_2=H, R_3=OEt,R_4=H (127) R_1=OEt, R_2=H, R_3=H,R_4=OEt



(128) R_1=H, R_2=OEt, R_3=OEt, R_4=H



(129) R=H (130) R=HO (131) R=



(132) R=

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