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Title:	**Review of Pharmacological Activity of Ephedra Gerardiana**
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Review of Pharmacological Activity of Ephedra Gerardiana

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ABSTRACT

Ephedra gerardiana (E. gerardiana,), commonly known as "Ma-huang," is a medicinal plant native to the Himalayan region. Historically, it has a long traditional use in various indigenous systems for medicinal purpose. The current review aims to summarize the present knowledge on the botanical description, phytochemistry, traditional uses, and pharmacological properties of *E. gerardiana*. This study was thoroughly based on previous literature and was conducted by using electronic databases such as PubMed, Scopus, and Google Scholar. Relevant studies and recently published articles up till 2020 were included in this review. *E. gerardiana* is a small shrub-like plant characterized by jointed stems, scale-like leaves, and cylindrical cones. It belongs to the family Ephedraceae and is commonly found in arid and semi-arid regions. Phytochemical analysis has revealed the presence of various bioactive compounds in Ephedra gerardiana, including ephedrine, pseudoephedrine, norephedrine, and methyl ephedrine. These alkaloids are primarily responsible for their pharmacological activities. In traditional medicine, Ephedra gerardiana has been used for its bronchodilatory, diaphoretic, diuretic, and thermogenic properties. Additionally, it has been employed for the treatment of respiratory disorders, namely, asthma and nasal congestion, as a stimulant. Its bioactive alkaloids, particularly ephedrine, have been extensively studied for their potential therapeutic applications. However, caution should be exercised due to the potential side effects associated with ephedrine-containing products. Further research can explore its mechanisms of action, optimize dosage regimens, and investigate potential drug interactions to ensure its safe and effective use in clinical settings.

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Keywords: botanical description, *Ephedra gerardiana*, Ma-huang, phytochemistry, pharmacological properties, traditional uses

1. INTRODUCTION

Ephedra gerardiana is a herbal drug, which contains many useful features. This herbal drug has many medicinal uses. It belongs to the family of Ephedraceae and its plant is approximately 1-4 feet long. It has red berries because of this; the plant becomes more beautiful and attractive.

The red colour of berries is due to the presence of their chemical constituent Flavonones.

According to the Unani system of medicine temperament of ephedra is hot and dry in a second order. In the Unani system of medicine drugs, which belong to second-order temperament, are used to treat phlegmatic disorder more easily and rapidly.

The pharmacological activities include anti-inflammatory, alterative, diuretic, expectorant, anti-inflammatory, and bronchitis.

The most effective action of this herbal drug is on our respiratory system. In Chinese medicine, it is also known as Mahaung.

Its most important biomarkers are Ephedrine and Pseudo-ephedrine.

The plant parts, which are used in medicine, are branches, flowers, and fruits.

2. METHODOLOGY

Different online databases were examined to highlight the therapeutical potential of *Ephedra gerardiana*, including Springer-Link, Google, PubMed, MEDLINE Data, Wiley Online Library, Science Direct, and Google Scholar. Data were searched using different keywords, such as pharmacological/biological activities, chemical constituents, morphology, habitat, characteristics, and `distribution of *Ephedra gerardiana*.

2.1. Pharmacognostic Features

Latin Name: *Epheragerardiana* Wall, *Ephedra vulgaris*
Family: Epheraceae.
Arabic Name: ZanbulKhail.
Urdu Name: Somkalpana, Masania, Narom, Somkalpa
English Name: Ephedra, Joint Pine, Brigham Tea.

Hindi Name: Som, Tutgantha.

2.2. Characteristics

It is a small shrub, which grows up to 1-4 feet. The stem of the plant has a nodule with dark green branches.

The leaves are small and round. The flowers are 6-10 mm long and unisexual naturally. The fruit of the plant is sweet, round in shape, red in colour, and has 1-2 seeds.

2.3. Habitat

Endemic to the mountains of Afghanistan, Bhutan, Northem India, Nepal, Sikkim, and Tibet.

2.4. Chemical Constituent

In all types of herbal drugs, there are different chemicals, which give them different pharmacological activity and medicinal uses, along with different side effects.

The ephedra chemicals are:

lignans, flavonoids, pseudoephedrine, ephedrine.

The root contains spermine alkaloids, Phenylethylamine alkaloids, Polysaccharides, Catechols, Tyrosine Derivatives, and EphedranineA& B.

The most important chemicals are ephedrine and pseudo-ephedrine [1–3].

The chemical constituents , which are separated from the herbal plants are more than 145 including alkaloids, flavonoids, tannins, and polysaccharides. The compounds separated from each species are enlisted in Tables 1-4. Their chemical structures are given in Fig. 1–5.

Table 1. Alkaloids Different Species of the Genus Ephedra (the structures of main compounds are illustrated in Fig. 1)

Classification	Chemical name	Plant source	Ref
Macrocyclic spermine alkaloids	Ephedradine A (1)	E. sinica (root)	[4]
	Ephedradine B (2)	E. sinica (root)	[5]
	Ephedradine C (3)	E. sinica (root)	[5]

Classification	Chemical name	Plant source	Ref
	Ephedradine D (4)	E. sinica (root)	
Imidazole alkaloid	Feruloylhistamine (5)	E. sinica (root)	[6]
Amphetamine-type alkaloids	D(–)-Ephedrine (**6**)	*E.Sinica*,*E.nebrodensis*, *E. major*	[7]
	L(+)-Pseudoephedrine (**7**)	*E. sinica*, *E. nebrodensis*	[8]
	D(–)Norephedrine (**8**)	*E. sinica*, *E. nebrodensis*	[8]
	L(+)-Noreseudoephedrine (**9**)	*E. sinica*	[9]
	D(–)Methyl ephedrine (**10**)	*E. sinica*, *E. nebrodensis*	[8]
	L(+)-Methylpseudoephedrine(**11**)	*E. sinica*, *E. nebrodensis*	[10]
	Ephedroxane (**12**)	*E. sinica*	[11]
	3, 4-Dimethyl-5-pheyloxazolidine (**13**)	*E. sinica*	[11]
	2, 3, 4-Trimethyl-5-phenyloxazolidine (**14**)	*E. sinica*	[11]
	O-benzoyl-L(+)-pseudoephedrine (**15**)	*E. sinica*	[11]
	O-benzoyl-D(–)-ephedrine (**16**)	*E. aphylla*	
	Hordenine (**17**)		
Quinoline alkaloids	Transtorine (**18**)	*E. transitoria*	[12]
	6-Methoxykynurenic acid (**19**)	*E. pachyclada*ssp. *Sinaica*	[13]
	Kynurenic acid (**20**)	*E. pachyclada*ssp. *Sinaica*	[13]
	6-Hydroxykynurenic acids (**21**)	*E. foemine*assp. *Foliate*	[13]
	Ephedralone (**22**)	*E. Alata*, *E. aphylla*	[14]
Pyrrolidine alkaloid	*cis*-3, 4-Methanoproline (**23**)	*E. foemine*assp. *foliate* (seed)	[13]
Other alkaloids	Maokonine (**24**)	*E. sinica*(root)	[15]
	(±)-1-Phenyl-2-imido-1-propanol (**25**)	*E. sinica*	[16]
	Tetramethylpyrazine (**26)**	*E. sinica*	[16]
	N-methybenzlamine (**27)**	*E. sinica*	[16]
	(2*S*,3*S*,4*S*)-2(carboxycyclopropyl)glycine (**28)**	*E. altissima*	[13]

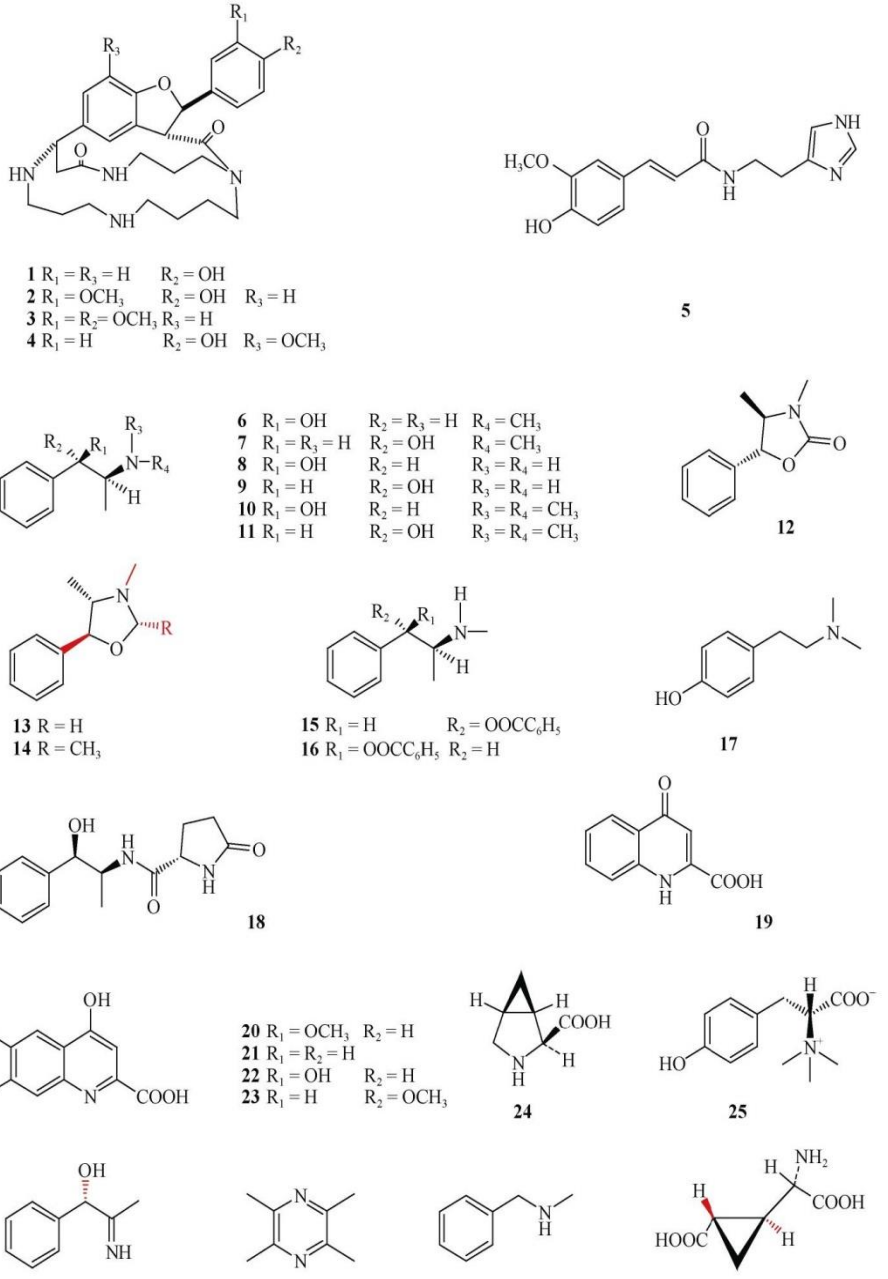
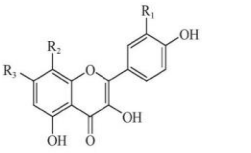


Figure 1. Structures of Different Alkaloids of *Ephedra*

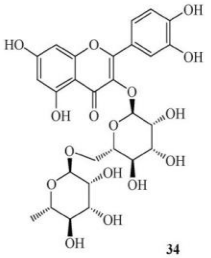
Table 2. Flavonoids of Different Species of the Genus *Ephedra* (the structures of main compounds are illustrated in Fig. 2)

Classification	Chemical name	Plant source	Ref.
Flavonols	Herbacetin (29)	*E. sinica*	[17]
	Kaempferol (30)	*E. sinica*(root)	[18]
	Quercetin (31)	*E. sinica*(root)	[18]
	Herbacetin 7-methyl ether (32)	*E. sinica*	[17]
	Rutin (33)	*E. campylopoda*	[9] [19]
	Herbacetin 8-methyl ether3-*O*-glucoside-7-*O*-rutinoside (34)	*E. alata*	[19]
	Herbacetin 7-*O*-(6″-quinylglucoside) (35)	*E. alata*	[19]
	Herbacetin 3-*O*-rhamnoside 8-*O*-glucoside (36)	*E. aphylla*	[20]
	Pollenitin B (37)	*E. sinica*	[20]
	Herbacetin-8-methyl ether 3-*O*-glucoside (38)	*E. sinica*	[20]
	Herbacetin 7-*O*-glucoside (39)	*E. sinica*	[20]
	Kaempferol 3-*O*-rhamnoside 7-*O*-glucoside (40)	*E. sinica*	[20]
	Herbacetin 7-*O*-neohesperidoside (41)	*E. sinica*	[20]
	Kaempferol-3-*O*-glucoside-7-*O*-rhamnoside (42)	*E. sinica*	[19]
	Kaempferol 3-*O*-rhamnoside (43)	*E. alata*	[19]
	Quercetin 3-*O*-rhamnoside (44)	*E. alata*	[9]
	Quercetin-3-*O*-glucoside (45)	*E. campylopoda*	
Dihydroflavonol	Dihydroquercetin (46)	*E. sinica*(root)	[18]
	3-Hydroxynaringenin (47)	*E. sinica*(root)	[18]
Flavonone	3′, 4′, 5, 7-Tetrahydroxy flavanone (48)	*E. sinica*(root)	[18]
	Naringenin (49)	*E. sinica*(root)	[21]
	Hesperidin (50)	*E. sinica*(root)	[22]

Classification	Chemical name	Plant source	Ref.
		E. sinica	
Flavanols	(–)-epicatechin (51)	*E. sinica E. nebrodensis*	[23]
	(–)-epiafzelechin (52)		[18]
	Catechin (53)	*E. sinica*(root)	[20]
	Afzelechin (54)		[18]
	Leucocyanidin (55)	*E. sinica*	[20]
	Symplocoside (56)	*E. sinica*(root)	[20]
		E. sinica	
		E. sinica	
Flavones	Tricin (57)	*E. sinica*	
	Luteolin (58)	*E. sinica*	[24]
	Apigeni (59)	*E. sinica*(root)	[25]
	3-Methoxyherbacetin (60)		[18]
	Apigenin-5-rhamnoside (61)	*E. sinica*	[24]
	6-*C*-glycosyl-chrysoeriol (62)	*E. sinica*	[24]
	Swertisin (63)	*E. sinica*	[26]
	Isovitexin-2″-*O*-rhamnoside (64)	*E. sinica*	[27]
	Apigenin-7-*O*-glucoside (65)	*E. sinica*	[20]
	Vitexin (66)	*E. campylopoda*	[9]
	Lucenin III (67)	*E. sinica*	[20]
	2″, 2‴-Di-*O*-*β*-glucopyranosyl-vicenin II (68)	*E. alata*	[19]
		E. aphylla	[28]
Anthocyan	Leucodelphinidin (69)	*E. sinica*	[29]
	Leucopelargonin(70)	*E. sinica*	[29]



30 R_1 = H R_2 = R_3 =OH
31 R_1 = R_2 = H R_3 = OH
32 R_1 = OH R_2 = H R_3 = OH
33 R_1 = H R_2 = OH R_3 = OCH_3



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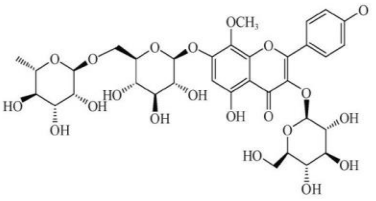

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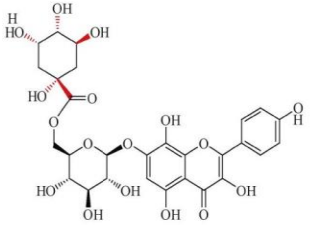

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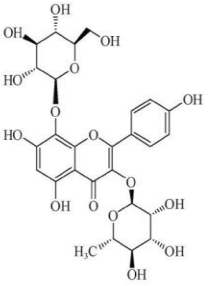

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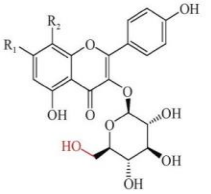
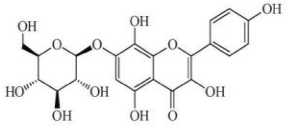


38 R_1 = OCH_3 R_2 = OH
39 R_1 = OH R_2 = OCH_3



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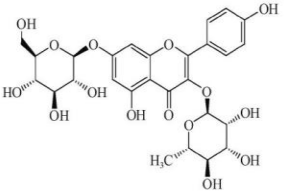

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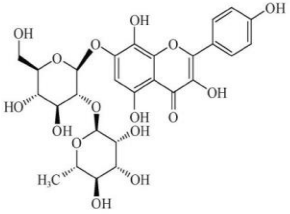

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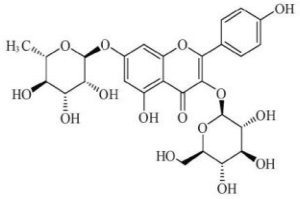

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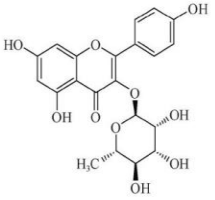

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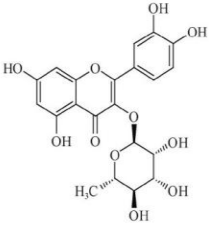

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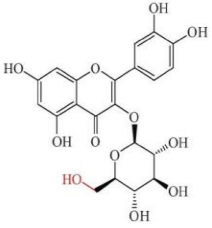
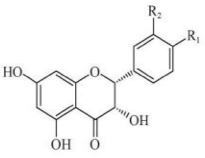
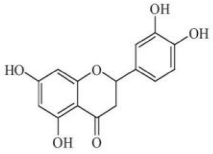
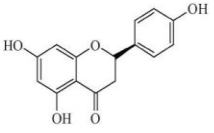








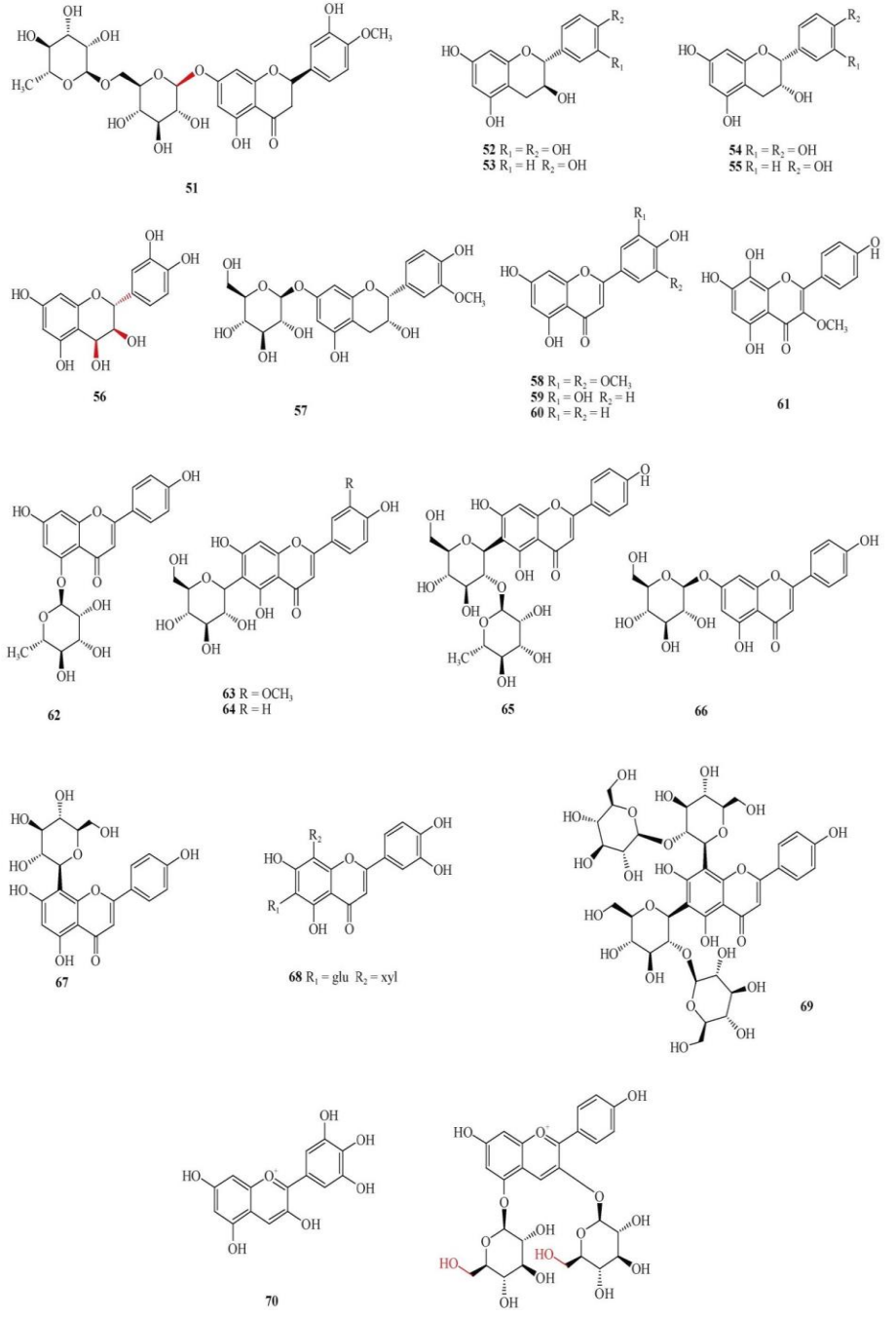
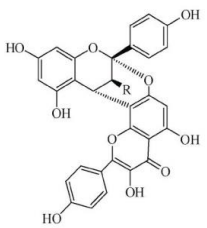


Figure 2. Structure of Different Flavonoids of *Ephedra*

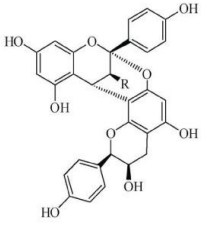
Table 3. Tannins of Different Species of the Genus *Ephedra*

Classification	ChemicalName	PlantSource	Ref
Dimer proanthocyanidins	Ephedrannin A(71)		
	Ephedrannin B (**72**)		
	Muhuannin A (**73**)	*E. sinica*(root)	[30]
	Muhuannin D (**74**)	*E. sinica*(root)	[30]
	Muhuannin B (**75**)	*E. sinica*(root)	[31]
	Muhuannin E (**76**)	*E. sinica*(root)	[30]
	Muhuannin C (**77**)	*E. sinica*(root)	[30]
	Muhuannin F (**78**)	*E. sinica*(root)	[30]
	Muhuannin G (**79**)	*E. sinica*(root)	[30]
	Muhuannin H (**80**)	*E. sinica*(root)	[32]
	Muhuannin I (**81**)	*E. sinica*(root)	[32]
	Muhuannin J (**82**)	*E. sinica*(root)	[32]
	Muhuannin K (**83**)	*E. sinica*(root)	[32]
	Ephedrannin D1 (**84**)	*E. sinica*(root)	[32]
	Ephedrannin D2 (**85**)	*E. sinica*(root)	[32]
	Ephedrannin D3 (**86**)	*E. sinica*	[33]
	Ephedrannin D4 (**87**)	*E. sinica*	[33]
	Ephedrannin D5 (**88**)	*E. sinica*	[33]
	Ephedrannin D6 (**89**)	*E. sinica*	[33]
	Ephedrannin D7 (**90**)	*E. sinica*	[33]
	Ephedrannin D8 (**91**)	*E. sinica*	[33]
	Ephedrannin D9 (**92**)	*E. sinica*	[33]
	Ephedrannin D10 (**93**)	*E. sinica*	[33]
	Ephedrannin D11 (**94**)	*E. sinica*	[33]
	Ephedrannin D12 (**95**)	*E. sinica*	[33]
	Ephedrannin D13 (**96**)	*E. sinica*	[33]
	Ephedrannin D14 (**97**)	*E. herb*	[33]
Trimer proanthocyanidins	Ephedrannin Tr1 (**98**)	*E. sinica*	[33]
	Ephedrannin Tr2 (**99**)	*E. sinica*	[33]
	Ephedrannin Tr3 (**100**)	*E. sinica*	[33]
		E. sinica	[33]

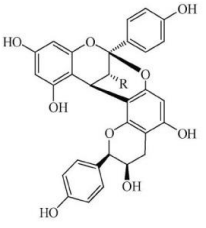
Classification	ChemicalName	PlantSource	Ref
	Ephedrannin Tr4	*E. sinica*	[33]
	(**101**)	*E. sinica*	[33]
	Ephedrannin Tr5	*E. sinica*	[33]
	(**102**)	*E. sinica*	[33]
	Ephedrannin Tr6	*E. sinica*	[33]
	(**103**)	*E. sinica*	[33]
	Ephedrannin Tr7	*E. sinica*	[33]
	(**104**)	*E. sinica*	[33]
	Ephedrannin Tr8	*E. sinica*	[33]
	(**105**)	*E. sinica*	[33]
	Ephedrannin Tr9	*E. sinica*	[33]
	(**106**)		
	Ephedrannin Tr10		
	(**107**)		
	Ephedrannin Tr11		
	(**108**)		
	Ephedrannin Tr12		
	(**109**)		
	Ephedrannin Tr13		
	(**110**)		
	Ephedrannin Tr14		
	(**111**)		
	Ephedrannin Tr15		
	(**112**)		
Tetramer proanthocya- nidins	Ephedrannin Te1 (**113**)	*E. sinica*	[20]
	Ephedrannin Te2 (**114**)	*E. sinica*	[20]
	Ephedrannin Te3 (**115**)	*E. sinica*	[20]
	Ephedrannin Te4 (**116**)	*E. sinica*	[20]
	Ephedrannin Te5 (**117**)	*E. sinica*	[20]



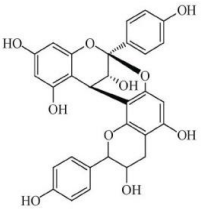
72 R = OH
73 R = H



74 R = OH
75 R = H



76 R = OH
77 R = H



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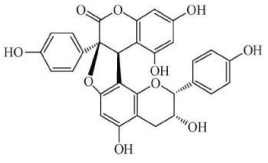

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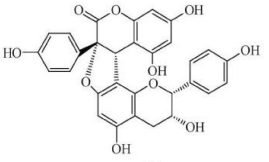

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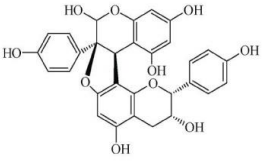

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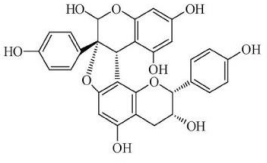

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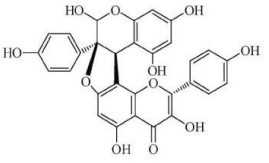

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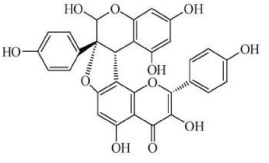

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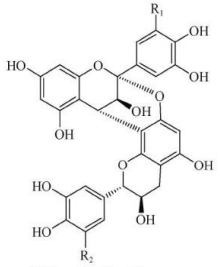

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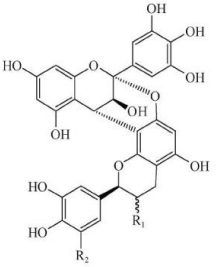
86 R_1 = OH R_2 = OH
87 R_1 = H R_2 = H



88 R_1 = —OH R_2 = H
89 R_1 = —OH R_2 = OH
90 R_1 = ····OH R_2 = OH
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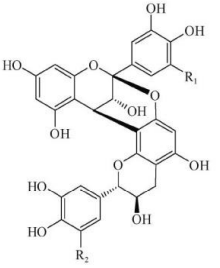

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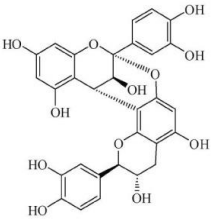
93 R_1 = OH R_2 = OH
94 R_1 = H R_2 = H



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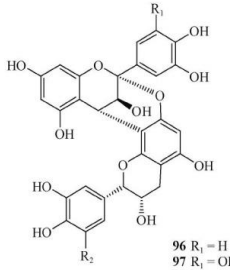
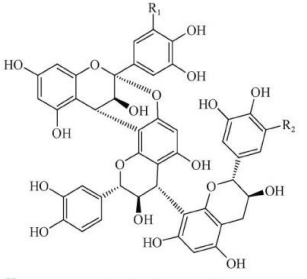
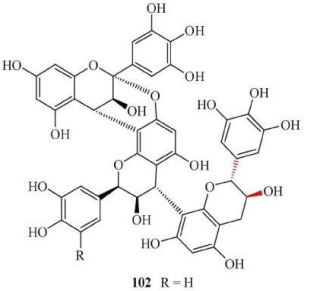


96 R_1 = H R_2 = H
97 R_1 = OH R_2 = H



99 R_1 = H R_2 = OH
100 R_1 = OH R_2 = H



102 R = H

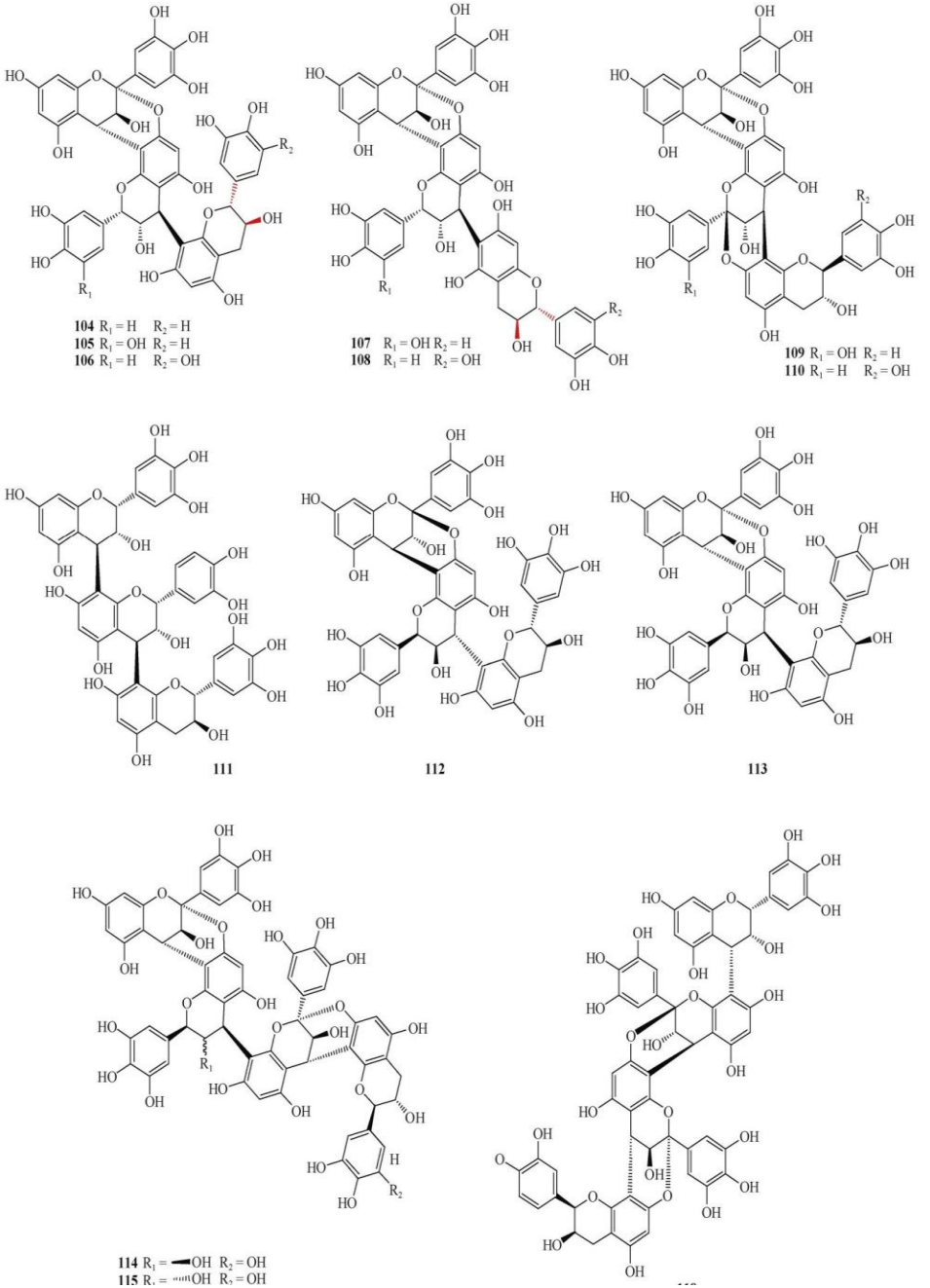


Figure 3. Different Tannins from *Ephedra*

3. PHARMACOLOGICAL ACTION

3.1. Cardiac Tonic

Ephedra is used as a cardiac tonic. It affects the CVS due to its biomarker Ephedrine, which is sympathomimetic amine activity. It increase the heart rate and also helps to manage low blood pressure to treat bradycardia, concerning hypotension. It also increases cardiac contractility mostly in hypotension conditions in which blood pressure usually droops [1].

A case of orthotic hypotension was observed in this condition having blood pressure, which suddenly dropped in the standing position, hence, use of infusion of ephedra very was considered effective in this condition in which the person's blood pressure became normal but it can not be used for a long time because it may also increase blood pressure [2, 34].

Ephedra has catechols constituents, which are alpha-receptor activity (vaso-constriction), due to which it can have vasoconstriction effects.

3.2. Respiratory System

Ephedra has two basic constituents' ephedrine and pseudoephedrine. Both of them gives a very good effect on the respiratory system. The constituents help to widen the lung's airway and also help to cure the nasal decongestant.

Additionally, they also help to treat asthma because these constituents have b-adrenergic receptors, which relax airway smooth muscles, hence, ephedra is noticed to be effective in asthma cases [2].

Ephedra has been effective in the respiratory system, especially in asthma that is why it is also known as DAMA BOTI.

3.3. Anti-Inflammatory

Ephedra also helped to reduce swelling. It has ephedranine A & B chemicals, which contain anti-inflammatory effects and reduce swelling, especially when applied in joint pain conditions like Rheumatoid Arthritis and Osteoarthritis. Paste of bark of ephedra should be applied on the affected area, which may give relief in pain and also in swelling [3].

Due to its effect on the joint, it is called Joint Pine.

3.4. Anti-Tumor Activity

Ephedra also has anti-tumor activity. It has two chemicals, namely, lignans, flavones both of which have anti-oxidant and anti-tumor properties, which suppress the growth of the tumor and also act as anti-bacterial medicine [2].

3.5. Renal System

Ephedra has another special property, which is Diuretic [1, 2].

It chemical ephedrine has multiple actions and one of them is Diuretic action. It produces a positive effect on renal system diseases such as renal calculi, urethritis, and UTI. , and those conditions in which dieresis is necessary through the kidney [1, 34]

3.6. Side Effects

Normally, any drug either it is herbal or synthetic, its excessive use can be harmful.

Prolong use of joint pine could elevate blood pressure because it has vasoconstriction property, which also helps to reduce lower blood pressure [2, 3].

It contraindicated in high blood pressure.

Some noticeable side effects include, vomiting, nausea, and minor abdominal pain [1, 35].

Some researches is also used in Obesity but in my point of view it not be useful for slimming medicine because it might be caused hypertension [1, 35].

4. CONCLUSION

Traditional medicine has employed *E. gerardiana* for its bronchodilatory, diaphoretic, diuretic, and thermogenic properties. The bronchodilatory effects of ephedrine have been extensively studied, leading to its inclusion in various over-the-counter medications for respiratory conditions. However, it is important to note that ephedrine-containing products have been associated with potential side effects and safety concerns. Adverse effects such as increased heart rate, elevated blood pressure, and central nervous system stimulation have been reported. Therefore, caution should be exercised when using E. gerardiana or

products containing ephedrine and it is advisable to consult with healthcare professionals before its usage. Further research is needed to elucidate the precise mechanisms of action of Ephedra gerardiana's bioactive compounds, optimize dosage regimens, and explore potential drug interactions. These studies would contribute to ensuring the safe and effective use of E. gerardiana in clinical settings and enhancing our understanding of its therapeutic potential. Concluding, E. gerardiana is a valuable medicinal plant but it should be used carefully, considering the potential risks associated with ephedrine-containing products.

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