SUPPORTING INFORMATION

Anticancer potential of the *Zanthoxylum* genus: A review of phytochemistry and bioactivity

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Abstract. The *Zanthoxylum* genus, belonging to the Rutaceae family, comprises over 250 species and is widely distributed across Asia, Africa, Europe, and the Americas. These species have been appreciated their significance as both spices and medicinal plants with broad therapeutic applications, especially for cancer treatment. *Zanthoxylum* species via *Z. nitidum*, *Z. armatum*, *Z. chalybeum*, *Z. bungeanum*, *Z. piperitum*, *Z. simulans*, *Z. capense*, *Z. schinifolium*, and *Z. zanthoxyloides* were a rich source of cytotoxic components, including crude extracts, essential oils, secondary metabolite compounds, such as alkaloids, flavonoids, lignans, and coumarins that showed potential anticancer agents through many different mechanisms. However, there are some reports on the safety/toxicology of some *Zanthoxylum* species, and advice about using them for a long time must be narrowly supervised, as well as further toxicity investigations to access their safety before *in vivo* trials.

Keywords: *Zanthoxylum*, anticancer, traditional use, extract, essential oil, secondary metabolites.

Classification numbers: 1.2.4, 5.1.2.

CONTENTS OF SUPPORTING INFORMATION

1. TABLE

Table S1. Traditional uses of *Zanthoxylum* species in Vietnam

No	Sciencetific name	Vietnamese name	Plant description	Distribution area	Parts used	Traditional uses	Ref.
1	*Zanthoxylum acanthopodium* DC.	Sẻn	Shrub 4 m tall; rachis winged; leaflets odoriferous, glabrous; coccus red.	Forest edge, 1,500-2,000 m altitude in Hoa Binh (Mai Chau), Kon Tum (Ngoc Linh), Binh Phuoc (Bu Dang), and Lâm Dong (Bidoup, Langbian)	leave, fruit	Fruits are used to treat dysentery, rheumatism, abdominal trauma causing overwork and stomach pain. The seeds are fragrant and bitter, cause dryness, and cool down.	[1-3]
2	*Zanthoxylum armatum* DC.	Sẻn gai	Shrub 4 m tall; rachis winged; leaflets glabrous; panicles on old branches; flowers whitish; coccus red, 4-5 mm diameter	Based on the current 1,300 m in Lao Cai (Sa Pa), Cao Bằng, Tuyen Quang (Ham Yen) and Ha Giang	roots, fruit, leaves	Seeds are used as pepper. Roots treat snake venom; Fruits and seeds are nutritious and diuretic, used to treat cold, toothache, stomachache, digestive disorders, *Ascaris suum* disease, headaches, coughs, flu, rheumatism, and poisonous snake bites. Leaves are used externally to treat collarbone, swelling, boils, and skin rashes. Dosage: 6-10g, decoction.	[1-3]
3	*Zanthoxylum avicennae* (Lamk.) DC.	Muồng truổng, Hoàng mộc dài, Màn Tàn, Sen lai, Tần	Shrub 8 m tall; rachis bearing numerous 2-4 cm long leaflets; flowers whitish; coccus 1-2; seeds black	Forests and mountains in Northern and South provinces, such as: Son	leave, roots, stem bark, fruit	Bitter bark nourishes and treats rashes and ulcers. It contains the alkaloid berberine. People often take the leaves for cooking, take the root or stem bark, peel them until golden, or dry them to make medicine. No other processing is required. People often take the	[1-4]

No	Sciencetific name	Vietnamese name	Plant description	Distribution area	Parts used	Traditional uses	Ref.
		tiêu, Buồn chuồn, Mú tương, Cam, Sẻn		La, Lang Son, Quang Ninh, Bac Giang, Vinh Phuc (Tam Dao), Ha Noi (Ba Vi), Hoa Binh (Kim Boi, Cho Ghenh), Thanh Hoa, Ha Tinh, Quang Binh (Ba Ren, Bo Trach, Dong Hoi), Thua Thien Hue, Da Nang (Ba Na), Quang Nam, Kon Tum		thick yellow star root and drink it to treat rashes, ulcers, and watery discharge. Take 6 to 12g of dry roots every day. Use externally, regardless of dosage, in bath water when having rashes, sores, or scabies. Some places use the leaves for cooking. People often take the leaves for cooking and use the roots or stem bark and root bark to treat rashes, ulcers, and scabies. In China, people use the roots to treat jaundice, hepatitis, emphysema, nephritis, rheumatism, tendon pain, brittle falls, and pain. The fruit is used to treat stomachache and cold. Leaves are used to treat collarbone, backache, mastitis, boils, and pyoderma. Dosage: 30-60g roots, fruits 3-6g, decoction form. Use crushed leaves or boiled boil leaves with water to bathe and wash rashes and scabies for external use. Prescription: 1. Chronic hepatitis: Use *Z. avicennae* roots, *Hypericum japonicum* (Cỏ ban), *Artemisia capillaris* (Nhân trần hao), *Plumbago zeylanica* (Bòi ngòi bò), each 15g, decoct and drink. 2. Osteoarthritis, collarbone: Use 30-60g *Z. avicennae* root, decoct and drink.	
4	*Zanthoxylum cucullipetalum* Guill.	Hoàng mộc cánh bầu	Shrub 5 m tall, branches sarmentous; leaflets thin, glabrous; flowers yellowish; follicles red; seeds black.	Ha Son Binh, Nha Trang, Phan Rang			[1]

No	Sciencetific name	Vietnamese name	Plant description	Distribution area	Parts used	Traditional uses	Ref.
5	*Zanthoxylum cuspidatum* Champ. ex Benth.	Đắng cay leo	Climbing shrub with branches with short, downward-curving thorns. Oddly pinnately compound leaves, with 13-17 pairs of leaflets growing alternately, unbalanced, the leaf axis sometimes has spines. Flowers form in clusters in the leaf axils. The capsule has 1-4 seeds, with a grooved outer layer and an easily separated parchment-like inner layer containing each black seed.	Northern and Central Vietnam forests from Cao Bang, Lang Son, Lao Cai, Ninh Binh, and Lam Dong	Fruit, leaves	The fruit has a bitter taste, aroma, and warm properties; it causes sweating, regulates menstruation, and reduces fever. Use the fruits to reduce swollen; use leaves to treat leprosy (Hansen's disease).	[2]
6	*Zanthoxylum evodiaefolium* Guill.	Sẻn lá dấu dầu, Hoàng mộc phi, Đắng cay ba lá	Shrub to 8 m tall; petiole short; leaflets 3; flowers white; coccus 8 mm long.	Khanh Hoa (Vong Phu, Nha Trang) and Lam Dong (Di Linh, Braian)	fruit	Infuse ethanol with fruits and seeds to drink in treating cold, stomachache, vomiting, cholera, and dysentery or chew the fruit to treat bleeding gums. The fruit is used to help digestion, treat worms, toothache, and sometimes mixed with water to make it fragrant	[1, 2, 4]
7	*Zanthoxylum laetum* Drake.	Hoàng mộc sai	Shrub 3-4 m tall; leaflets thin, glabrous; follicles 6-7 mm long.	Cao Bang, Lang Sơn, Hoa Binh, Ninh Binh, Da Nang			[1, 3]
8	*Zanthoxylum myriacanthum* Wall. ex Hook. f. (*Zanthoxylum*	Hoàng mộc nhiều gai	Treelet or tree 10 m tall; pricks numerous, red; flowers white; styles 4, connate	High mountain areas at 500-2100m altitudes in	Seed, root, leaves	The seeds are used as a spice. the fruit is used as a spice. Roots and leaves are used to treat cold, rheumatism, collarbone, boils, itch, bleeding wounds, and fire burns.	[1, 2]

No	Sciencetific name	Vietnamese name	Plant description	Distribution area	Parts used	Traditional uses	Ref.
	rhetsoides Drake)			Cao Bang, Lao Cai (Sa Pa), Thai Nguyen, Ha Noi (Ba Vi), and Lam Dong (Bao Loc)			
9	*Zanthoxylum multijugum* Franch.		The species is morphologically most similar to *Z. scandens*: stem woody sarmentose, midvein without spine and a leaf with more than 10 leaflets. However, the species can be differentiated from *Z. scandens* by characteristics of the leaflet (base rounded; apex obtuse, acuminate, rounded, mucronate).	Ha Giang			[5]
10	*Zanthoxylum nitidum* (Lamk.) DC.	Hạt sẻn, Sang, Sang láng, Sẻn, Xuyên tiêu, Hoàng liệt, Hoa tiêu, Hoa tiêu thích, Sơn hồ tiêu thích, Ba tiêu, Sưng, Trưng,	Sarmentous; leaflets glabrous; flowers unisexual; seeds black.	Grows wild everywhere in our country, most commonly in mountainous provinces such as Lao Cai, Son La, Cao Bang, Ha Giang (Vi Xuyen), Lang	root, branch, fruit, bark, leaf, stems	Roots and fruits use to be antipyretic, improve digestion, treat hemorrhoids, and rheumatism; fruits are used as spices. According to ancient papers, it is spicy, warm, and poisonous and has effect of the lung, spleen, and kidney. It force out cold, reduces inflammation, and disinfects; treat cold, stomach pain, diarrhea, and deworming. Folk use: The fruit is used medicinally under the name “hoa tiêu” or “thục tiêu” to help digestion, treat worms, toothache, and sometimes mixed with water to make it	[1-4]

No	Sciencetific name	Vietnamese name	Plant description	Distribution area	Parts used	Traditional uses	Ref.
		Hoàng lực, Dã hoa tiêu, Lưỡng diện châm, Lưỡng phù chấm, Xuyên tiêu		Son, Yen Bai, Bac Can, Quang Ninh, Thai Nguyen (Dong Hy), Phu Tho, Hoa Binh, Ha Noi (Son Tay, Thu Phap, Ba Vi, Phu Lo), Ninh Binh, Nghe An Ha Tinh, Quang Binh (Bo Trach) Quang Tri, Da Nang (Tourane), Dak Lak (Dak Mil), Khanh Hoa (Nha Trang, Ninh Hoa), Lam Dong (Da Lat), Ho Chi Minh		fragrant. Use 3-5g daily as a decoction. External use regardless of dosage. Note: 1. People also use this plant cheaply with the name "Hoàng lực" or "Sưng" roots or "Huỳnh lực" as medicine to treat fever, hyperhidrosis, chronic malaria, and rheumatism. Use 4-8g daily as a decoction or infusion with ethanol. Berberine is found in the roots of "Sưng". 2. Roots (and root bark) are used to treat: 1. Arthralgia, swollen, backache, rheumatism, collarbone; 2. Epigastric pain, toothache, sore throat; 3. Snakebite, pyoderma, dermatitis, tetanus. Dosage: 9-15g roots; l.5-3g root barks, decoct and drink. For external use, apply fresh root bark or powdered dry bark. Use root decoction or infuse ethanol with roots to treat tooth decay in which patients are avoid eating sour foods. 3. The fruit treats cough, sore throat, rhinorrhea (runny nose), stomachache, vomiting, diarrhea, malaria, backache, rheumatism, toothache, snakebite and roundworm, and uterine bleeding. Use 3-5g fruits in decoction or powder daily. 4. Leaves are used as a spice or make soup like Muồng Truổng (*Zanthoxylum avicennae* (Lam) DC.) and also apply to treat collarbone or boil with water to bath that is good for health.	

No	Sciencetific name	Vietnamese name	Plant description	Distribution area	Parts used	Traditional uses	Ref.
11	*Zanthoxylum rhetsa* DC.	Hoàng mộc hôi, Cóc hôi, Vàng me, Xong, Sẻn hôi	Tree; leaflets lanceolate, 10-15 cm long; inflorescence pubescent; follicles; seeds black	Vinh Phuc, Phu Tho, Da Nang (Tourane), Khanh Hoa (Nha Trang, Vong Phu), Dak Lak (Dak Mil, Krong Pak), Lam Dong (Da Lat), Dong Nai (Bien Hoa)	Seed, root, bark	It has bitter and aromatic qualities that are used to make beer; Bark nourishes, calms livestock, reduces heat, treats rheumatism, and treats bronchitis, asthma, and excessive salivation (a part of the image, according to Pierre). The seeds are used to treat flatulence, diarrhea, and rheumatism. They are also used as a spice instead of pepper, often preserved in vinegar. Seed essential oil is used to treat cholera; root bark is used to destroys or forces out roundworms. The bark is used to treat diarrhea, malaria, rheumatism, and stomach disorder. The aromatic gum of leaves is also used to make beer instead of yeast. Young leaves are often used as a spice.	[1, 2]
12	*Zanthoxylum planispinum* Sieb. et Zucc. (*Z. alatum* Roxb. var. *planispinum* Rehd. et. Wils)	Đắng cay	Small tree up to 4m tall, with many branches, with long and hanging branches that are completely smooth. Branches have flat, straight, or nearly straight spines. Leaves are pinnately compound, alternate, consisting of 3-5 sessile leaflets; the middle part of the standard stem has wings; the upper leaflets are more prominent; the lateral leaves do not need to be at the base; glands are small, black below, opaque, with few large clear glands.	In northern provinces of Vietnam, the trees grow in Lao Cai and Cao Bang.	Fruit, seed, root	Fruits and seeds are used to treat fever, stomachache, vomiting, dyspepsia, diarrhea, arthralgia, rashes, and wet cough. They can infuse ethanol with fruits and seeds to drink, or drink with a dose of 4-8g. The fruits is also used to chew and suck in reducing the toothache. People often process root to treat rashes, ulcers, and watery discharge.	[2, 4]

No	Sciencetific name	Vietnamese name	Plant description	Distribution area	Parts used	Traditional uses	Ref.
			Inflorescences are sparse in the leaf axils, and the flowers are greenish-white. The fruit is a capsule, has a nymph, is open, 5mm large, red-brown in color, has fragrant glands and protruding bumps, and the outer shell is easy to separate from the inner shell. Seeds are solitary, spherical, and jet-black. Flowers in May-June, fruits in August-September.				
13	*Zanthoxylum scabrum* Guill.	Dây khắc dung	Sarmentous to 10 m tall; branches rufous pubescent; flowers white; follicles 5-6 mm large; seeds black.	Ha Son Binh, Thanh Hóa			[1]
14	*Zanthoxylum scandens* BL.	Hoàng mộc leo, Đắng cay	Spreading shrub; rachis sometime pricky; stamens longer than petals; follicles 6 mm long; seeds black	Son La, Lao Cai (Bac Ha), Lang Son, Hoa Binh (Mai Chau), Ha Noi, Ninh Binh, Quang Tri, Lam Dong (Langbian, Di Linh)	fruit	Bitter seed causes dryness, reduces heat, and benefits menstruation.	[1, 3]

Table S2. Traditional uses of Zanthoxylum species in the other countries

No	Species	Traditional uses	Country	Ref.
1	*Zanthoxylum acanthopodium*	Fruits used as aromatic substances and as spices, tonic, treat dysentery, treat paralysed and skin diseases such as abscess and leprosy.	Indonesia	[6-8]
		Used as a spice and traditional medicine to treat fever, flu, colic, diarrhea, stomachache, toothache, injury, insect stings, in food processing.	Indonesia, China, Myanmar	[9]
2	*Zanthoxylum ailanthoides*	Treatment of myocardium disorder attenuation, bone-injury alleviation and cold resistance; treatment of heart disease, bone-injury and cold resistance.	China	[10, 11]
3	*Zanthoxylum alatum*	Used as an traditionally ethnomedicine for cancer in north-eastern india and south-east asia in the form of infusion and decoction at the dose of 1–2 oz (2, 3).	India	[12]
4	*Zanthoxylum americanum*	Used as herbal preparation from different parts for treating tumors, fungal skin infections, respiratory, urinary, genital and gastrointestinal (GIT) diseases by herbal healers.	Canada, United States	[13, 14]
5	*Zanthoxylum armatum*	The leaves, stem, bark, fruits, seeds and roots possess medicinal properties and are used in indigenous medicine preparation against various diseases like asthma, bronchitis, indigestion, varicose veins, diarrhea, rheumatism, dyspepsia, cholera and toothache.	India	[15]
		The aerial parts are used in management of fever, dyspepsia, stomachic upset, cholera, and in tooth- ache. The small branches are used as tooth brush (miswak) for washing the teeth while the powder of fruit is applied in toothache.	Pakistan	[16, 17]
		The leaves, fruits, stem, bark, seeds have been used in several indigenous medicinal practices as carminative, antipyretic, appetizer, stomachic, toothache, dyspepsia.	Nepal	[18]
6	*Zanthoxylum austrosinense*	As a folk medicinal plant named “Sou Shan Hu” in Guangxi Zhuang Autonomous Region of China, *Zanthoxylum austrosinense* shows the medical functions of expelling wind, detoxifying, relieving exterior syndrome, removing blood stasis and reducing swelling, and is used for the treatment of rheumatic bone pain and bruises.	China	[19]
7	*Zanthoxylum budrunga*	The aqueous extract of the leaves has a folkloric reputation for treating dyspepsia and some forms of diarrhea. The bark juice is used in dysentery, cough, headache and vomiting.	India	[20]
	Zanthoxylum buesgeniiare	In Sierra Leone, roots are used as remedy to cure venereal diseases, arthritis, and rheumatism whereas leaves and barks are employed to treat leprosy and to relieve	Sierra Leone, Cameroon	[21]

No	Species	Traditional uses	Country	Ref.
		pain. In South West Region of Cameroon, it helps patients as aphrodisiac decoction and to increase sperm count.		
8	*Zanthoxylum bungeanum*	As early as the period of the pre-Qin Dynasty, the pericarps of *Z. bungeanum* have commonly been used as a special spice in important activities, with this being the earliest utilization of *Z. bungeanum* in folk life. The pharmacological effects of this plant were first listed in Shennong Bencaojing (the earliest Traditional Chinese Medicine (TCM) monograph during the Eastern Han Dynasty); it was used as an herbal medicine with the function of strengthening teeth, improving eyesight, and removing cold-dampness. In Zhenglei Bencao, another famous monograph on traditional Chinese medicine, *Z. bungeanum* was described as a treatment for throat impediment, vomiting, and postpartum abdominal pain, and in the Compendium of Materia Medica (Bencao Gangmu), *Z. bungeanum* pericarps were described as a good treatment for toothache, diarrhea, ascariasis, swelling, dampness, and others. In addition, *Z. bungeanum* was also recorded in other classic monographs of medicine including Yaoxinglun, Shiliao bencao, Bencao xinbian, Bencao tujing and others. The pericarps are attributive to the heart and spleen meridians with the properties of being pungent in taste and warm in nature. *Z. bungeanum* has a warming action, thus relieving pain, dispelling dampness, stopping diarrhea, and preventing itching; therefore, it can be applied to treat abdominal pain, toothache, vomiting, diarrhea, ascariasis, and other diseases caused by cold and dampness. Since 1977, it has been listed in the Pharmacopoeia of the People's Republic of China (Ch. P), and over 30 prescriptions containing *Z. bungeanum* have been applied for the treatment of abdominal pain, toothache, dyspepsia, vomiting, diarrhea, ascariasis, eczema, etc. In 2002, the Chinese Ministry of Health officially approved ZBM as a dietary medicinal herb to endorse public health (National Health and Family Planning Commission of the People's Republic of China, 2002).	China	[14, 22-24]
9	*Zanthoxylum capense*	Use in traditional medicine to treat mouth ulcers, toothache, flatulent colic, bronchitis, fever and infertility. It has also found application in the management of epilepsy (root part) and Human Immunodeficiency Virus (HIV).	South African	[25]
		Roots are traditionally used to treat violent chronic coughing, tuberculosis, bronchitis.	Mozambique	[26]
10	*Zanthoxylum chalybeum*	People of the state of Rondônia use the tea from leaves and roots to relieve toothache and to treat malaria.	Brazil	[27]

No	Species	Traditional uses	Country	Ref.
		The leaf decoction is used for the treatment of oedema in kwashiakor, while the root bark is used for the treatment of chest pains, malaria, colds, coughs and dizziness, for joint haemorrhagic septicaemia and helminthiansis in livestock. The fruits are used for chest pain, fever and sore throat, the leaves for snake bite. The leaves are commonly utilized by Embu community for the management of malaria.	Kenya	[28, 29]
		Used for management of tuberculosis and cough related infections and treating various opportunistic infections in HIV, malaria, sickle cell disease, measles, skin infections, jaundice, yellow fever and coughs.	Uganda	[30, 31]
11	*Zanthoxylum clava-herculis*	Used for the relief of toothache.	Canada	[13]
12	*Zanthoxylum gilleti*	Used for the management of tuberculosis, pneumonia, management of related bacterial diseases such as cold, stomachache, rheumatism and urinary infections in Ivory Coast.	Kenya	[31]
13	*Zanthoxylum integrifoliolum*	Used the bark as a remedy for snakebite and dyspepsia and as an aromatic tonic in fever.	Taiwan	[32, 33]
14	*Zanthoxylum leprieurii*	Used for the treatment of a wide range of disorders, including toothache, urinary and venereal diseases, rheumatism and lumbago.	Nigeria, Cameroon, Ghana, Sierra Leone	[34]
		The leaves, stems and roots are used in the treatment of gonococci, urinary infections, dysentery, arthritis, leprosy, stomachache and venereal diseases, the fruits are used in the treatment of stomach disorders, managing fever, malaria, tumors and sickle cell anemia, the infusion from the fruits is taken for the treatment of sickle cell anemia. The roots and stem barks are also used in ethnomedicine for the treatment of stomach disorders, gonorrhea, intestinal parasites and sterility.	Cameroon	[14, 35, 36]
		Used in the treatment of tuberculosis, malaria, human immunodeficiency virus (HIV) and several types of bacterial infection.	Uganda	[14, 31]
15	*Zanthoxylum liebmanniaum*	The stem barks are used for the treatment of stomach aches, amebiasis, and intestinal parasites and as a local anesthetic agent.	Taiwan, Sri Lanka, Mexico	[33]
16	*Zanthoxylum nitidum*	For more than 1,000 years in traditional Chinese medicine, and its fruit has been used as a spice. Traditional Chinese medicine (TCM) holds that *Z. nitidum* can relieve pain, disperse wind to dredge collaterals, promote blood circulation to	China	[37-41]

No	Species	Traditional uses	Country	Ref.
		remove blood stasis and remove toxicity to achieve detumescence; thus, it could be effectively applied in the treatment of stomach ache, toothache, rheumatic arthralgia, traumatic injury and venomous snake bites (China Pharmacopoeia Commission, 2015). The roots are widely used to treat rheumatism, toothache, neuralgia and swelling of the throat. Additional medical applications include the treatment of inflammatory diseases, various types of cancer, bacterial and viral infections, gastric and oral ulcers, and liver damage. Stewing pork leg bone with *Z. nitidum* has a good effect in the treatment of chronic lumbar muscle strain. The decoction of dry *Z. nitidum* roots and grinding fresh *Z. nitidum* roots with wine for external application can cure snake bites. The decoction of the root bark of *Z. nitidum* and eggs can be used to treat rheumatic bone pain. At present, a few daily necessities containing *Z. nitidum* extract are commercially available in the market, such as toothpaste, mouthwash, hand sanitiser, soap and shampoo. The most popular of these products is *Z. nitidum* toothpaste, which can eliminate toothache, freshen the breath, relieve gingival redness and swelling, and improve oral problems. *Z. nitidum* toothpaste has been sold in China for 40 years and is still a popular product. Moreover, *Z. nitidum* toothpaste is the first Chinese medicine toothpaste that has been approved by the Food and Drug Administration.		
17	*Zanthoxylum paracanthum*	Used for a long history as a traditional medicine in the areas where it is found. Communities living in the coastal areas of Kenya use stem and root extracts of this plant in the management of tumors and other related diseases, but thus far, only stem extracts have been chemically profiled.	Kenya,	[42, 43]
		The leaves are used as an indigenous vegetable, as they have a high nutrient content and it is claimed they cure gastrointestinal problems such as diarrhoea.	Tanzania	[42]
18	*Zanthoxylum piperitum*	Used as a spice to produce a fresh flavour as an ingredient of some spice mixes or to suppress unpleasant fishy and meaty odour.	Japan	[44]
		Used for edible and medicinal purposes as well as an anti-inflammatory agent.	Korea, China	[45]
19	*Zanthoxylum rhetsa*	The fruits and stem barks are used in the treatment of asthma, bronchitis, heart complaints and rheumatism. The essential oils are used to treat cholera, rheumatism, eczema, dandruff, and are also used as an antiseptic, astringent and disinfectant.	Bangladesh	[46]

No	Species	Traditional uses	Country	Ref.
		The plant is routinely used in food and medicine. The roots are consumed as food by indigenous people of northeast India and in many cuisines, fruits are used as spice. Traditionally, the plant is employed for treatment of intestinal worms, urinary infection, heart troubles, toothache, asthma, bronchitis, and rheumatism; the bark are used to treat cardiac, respiratory diseases, tooth infection, stomach infection and rheumatism. The Naga tribes in the northeastern region of India employ the leaf decoction in the treatment of intestinal worm infections, deworming and as insecticide. A paste from the spine of this plant is used by Kannikar tribes in India to relieve breast pain and increase milk in breastfeeding women. Adi tribe uses the tender shoots of the plant as food. The fruit essential oils and bark are also used as an antidiabetic, antispasmodic, and diuretic agent by Kerala people in India.	India	[47, 48]
		The roots, bark and leaves of *Zanthoxylum rhetsa* (Roxb.) DC. are used in various medicinal preparations for example paste made from the hard spines of *Z. rhetsa* is used as a pain relief and to increase lactation in nursing mothers. The bark has been reported to be a remedy for stomach and chest pains, and also to treat snake bite. The fruits and seeds of *Z. rhetsa* are used to treat toothache, dizzyness and bloating, malaria, urinary diseases and rheumatism. The leaf decoction is used to treat intestinal worm infections and as insecticide. The most popular domestic use of the root in Nigeria is as chewing stick to clean the mouth. Due to the warm, pungent and benumbing effect when chewed, the aromatic warm taste with profuse salivation is believed to be beneficial to the elderly and those with sore teeth and dental caries. Traditional healers have used different species of the *Zanthoxylum* for treatment of a wide range of disorders, including urinary and venereal diseases, rheumatism and lumbago. The bark decoction is used to treat chest pain and chewed bark applied as antidote for snake bites. The eastern Nigerians use the roots as chewing stick to treat dental caries.	Nigeria	[49]
		The powdered barks are mixed with oil and used as a formula to treat stomachache, the barks are used as a remedy for chest pain and snakebite and also as a sunscreen in industries. The fruits are used as spice, the fruit essential oils is known as “Mullilam oil” are used as anti-inflammatory, antiseptic, anticholera, diarrhea, hypocholesterolemic, mosquito repellent and soothing agent for dental caries.	Philippine	[49]

No	Species	Traditional uses	Country	Ref.
20	*Zanthoxylum rhoifolium*	Used in Amazonia for the treatment of skin eruptions, venereal diseases, and malaria; the leaf essential oil has shown antibacterial effects.	Cameroon	[50]
		The roots are used as a febrifuge, digestant and tonic. The stem barks are used to treat flatulence, colic, dyspepsia, ear aches, toothaches and snake bites.	Brasil	[51]
21	*Zanthoxylum schinifolium*	Used to invigorate the circulan of blood, and it was regarded as a drug for various pains. The fruit used for epigastric pain accompanied by cold sensation, vomiting, diarrhea, abdominal pain due to intestinal parasitosis, ascariasis, and eczema.	China	[14, 52]
		Used to treat several symptoms, cure for the common cold, stomach ache, diarrhea, and jaundice.	Korea, and Japan	[14, 53]
22	*Zanthoxylum simullans*	Used for the treatment of stomach ache, toothache, intestinal worms, eczema, and pruritus.	China	[54]
		Used for the treatment of malaria.	Brazil	[27]
23	*Zanthoxylum tetraspermum*	Used for the treatment of rheumatism and some forms of diarrhea. The barks are pungent, and sticks prepared from it are used for preventing toothache.	Sri Lanka	[33]
24	*Zanthoxylum usambarense*	Used for the treatment of malaria, upper respiratory tract infections, cough, rheumatism, tooth decay and sore gums.	Kenya	[55]
25	*Zanthoxylum xanthoxyloides*	Used for treatment of skin infections, urinary infections, and dysentery; the fruit essential oil exhibits antibacterial activity. The aqueous decoction of leaves and roots is used to wash wounds for healing. The root barks are useful in the treatment of intestinal worms and edema. A combination of roots and leaves of *Flacourtia flavescens, Uvaria chamae* and *Hibiscus surattensis* with the roots of *Z. zanthoxyloides*, is employed for the treatment of sickle cell anemia. The root barks of *Z. zanthoxyloides* mixed with the rhizomes of *Aframomum melegueta* relieves abdominal pain and hyperthermia. The traditional healers also treat the patients of stomach disorders with the fruits of this plant, extensively. Other uses of this plant include in digestion, diarrhea, urinary tractinfections and gingivitis. *Z. zanthoxyloides* is also traditionally used for the treatment of hemolysis of red bloodcells, which is a common feature in patients with malignant neoplastic diseases.	Cameroon	[14, 35, 36, 50]
		Z. zanthoxyloides (Lam.) Zepern and Timler is described for its broad spectrum of activities, viz. activity against sickle-cell anaemia.	Ghana	[56]

No	Species	Traditional uses	Country	Ref.
		The roots are used as antibacterial toothbrush in South Western Nigeria, the decoction of the leaves and roots is used to wash wounds for healing, the bark of the plant is used in the treatment of intestinal worms and edema.	Nigeria	[57, 58]

2. FIGURE

Zanthoxylum acanthopodium DC.

Zanthoxylum armatum DC.

Zanthoxylum avicenniae (Lam.)

Zanthoxylum evoidiifolium Guillaum.

Zanthoxylum laetum

Zanthoxylum myriacanthum Wall. ex Hook.f.

Zanthoxylum nitidum (Roxb.) DC.

Zanthoxylum rhetsa (Roxb.) DC.

Zanthoxylum scabrum Guillaum.

Zanthoxylum scandens Blume

Figure S1. *Zanthoxylum* species in Vietnam *[59]*

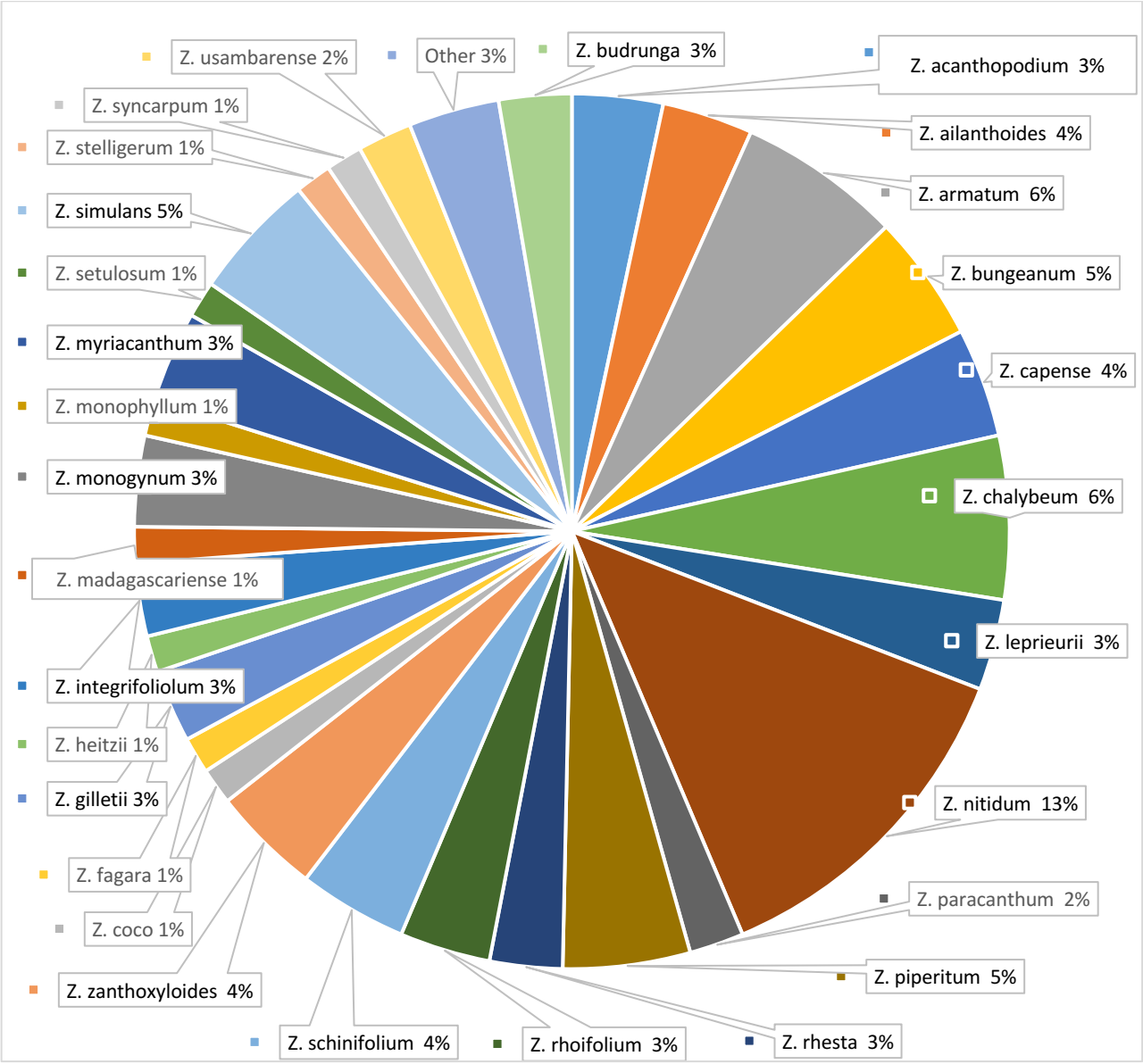
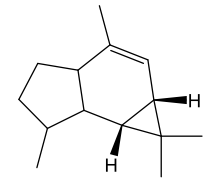
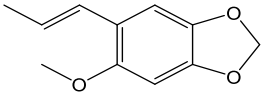


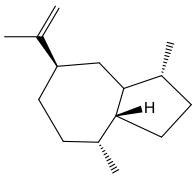
Figure S2. Statistics of studies on anticancer and cytotoxicity of the *Zanthoxylum* genus



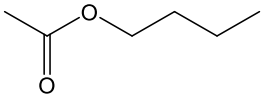
dehydroaromadendrane



(E)−carpacin

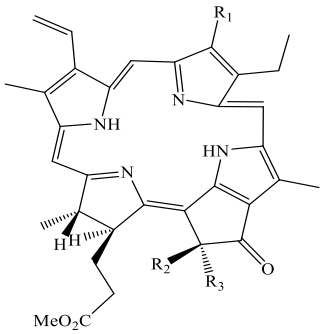


γ-gurjunene

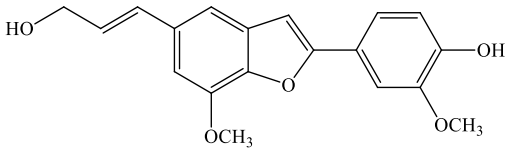


butyl acetate

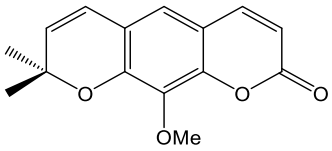
Figure S3. Anticancer and cytotocxic compounds isolated from *Zanthoxylum acanthopodium*



pheophorbide-a methyl ester (**1**): R_1=CH_3, R_2=H, R_3=CO_2CH_3
pheophorbide-b methyl ester (**2**): R_1=CHO, R_2=H, R_3=CO_2CH_3
13^2-hydroxyl (13^2-S) pheophorbide-a methyl ester (**3**): R_1=CH_3, R_2=OH, R_3=CO_2CH_3
13^2-hydroxyl (13^2-R) pheophorbideb methyl ester (**4**): R_1=CHO, R_2=CO_2CH_3, R_3=OH

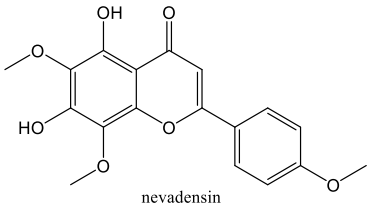


ailanthoidol

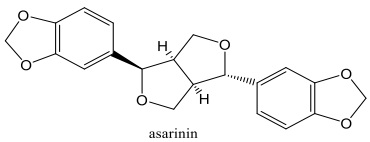


luvangetin

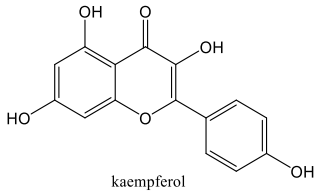
Figure S4. Anticancer and cytotocxic compounds isolated from *Zanthoxylum ailanthoides*



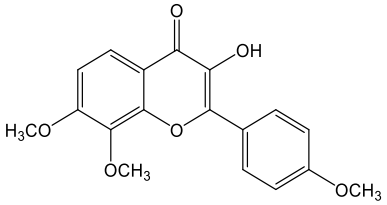
nevadensin



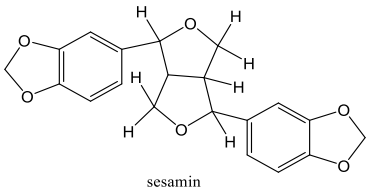
asarinin



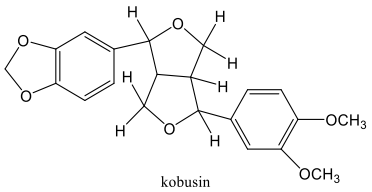
kaempferol



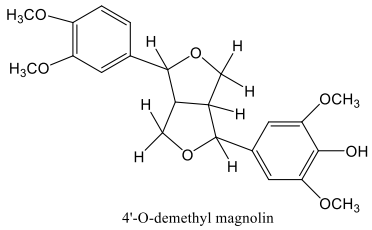
tambulin (3,5-dihydroxy-7,8,4’-trimethoxyflavone)



sesamin

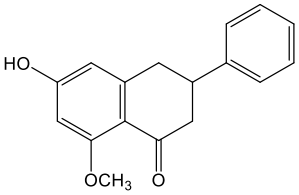


kobusin

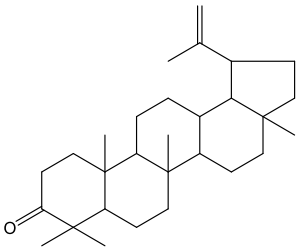


4'-O-demethyl magnolin

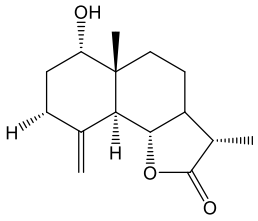
Figure S5. Anticancer and cytotocxic compounds isolated from *Zanthoxylum armatum*



5-methoxy-7-hydroxy flavonone

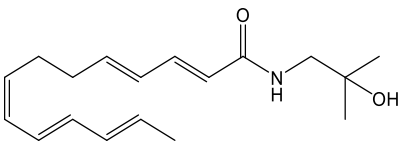


lup-20-(29)-1-en-3-one

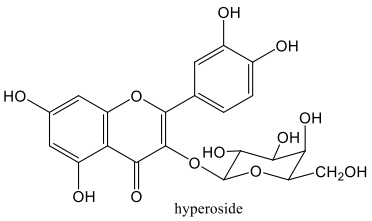


11β-13-dihydro-1-epireynosin

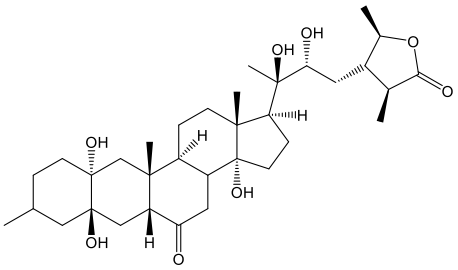
Figure S6. Anticancer and cytotocxic compounds isolated from *Zanthoxylum budrunga*



hydroxy-γ-sanshool

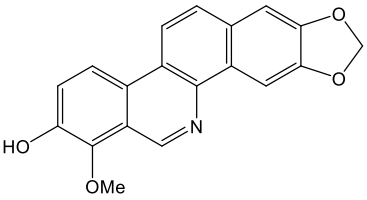


hyperoside

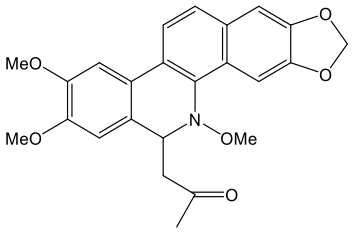


bungsteroid A

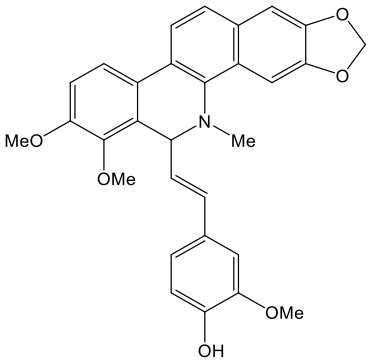
Figure S7. Anticancer and cytotocxic compounds isolated from *Zanthoxylum bungeanum*



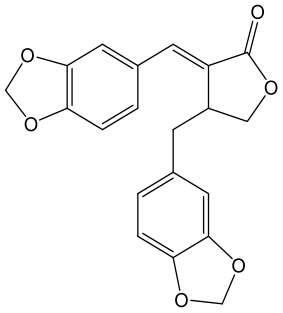
decarine



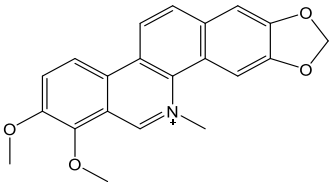
6-acetonyldihydronitidine



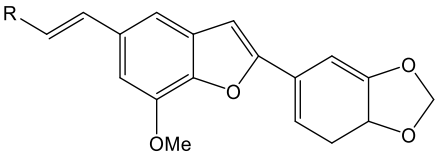
zanthocapensine



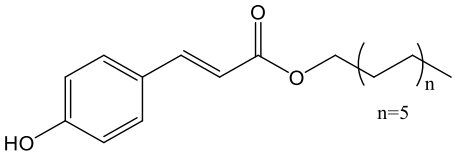
(–)-savinin



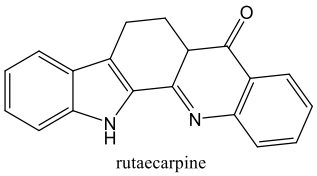
chelerythrine



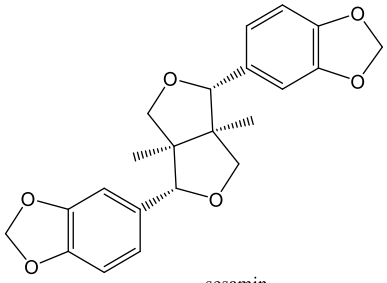
R=CH_2OH: zanthocapensol
R=$COOCH_3$: zanthocapensate



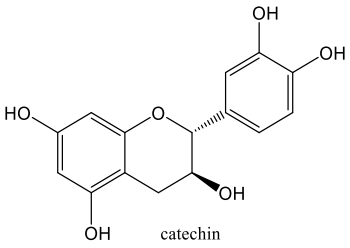
dodecyl-trans-p-coumarate



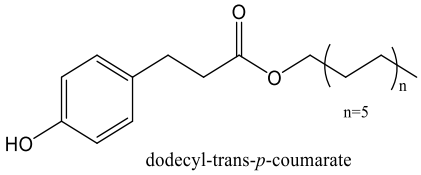
rutaecarpine



sesamin



catechin



dodecyl-trans-*p*-coumarate

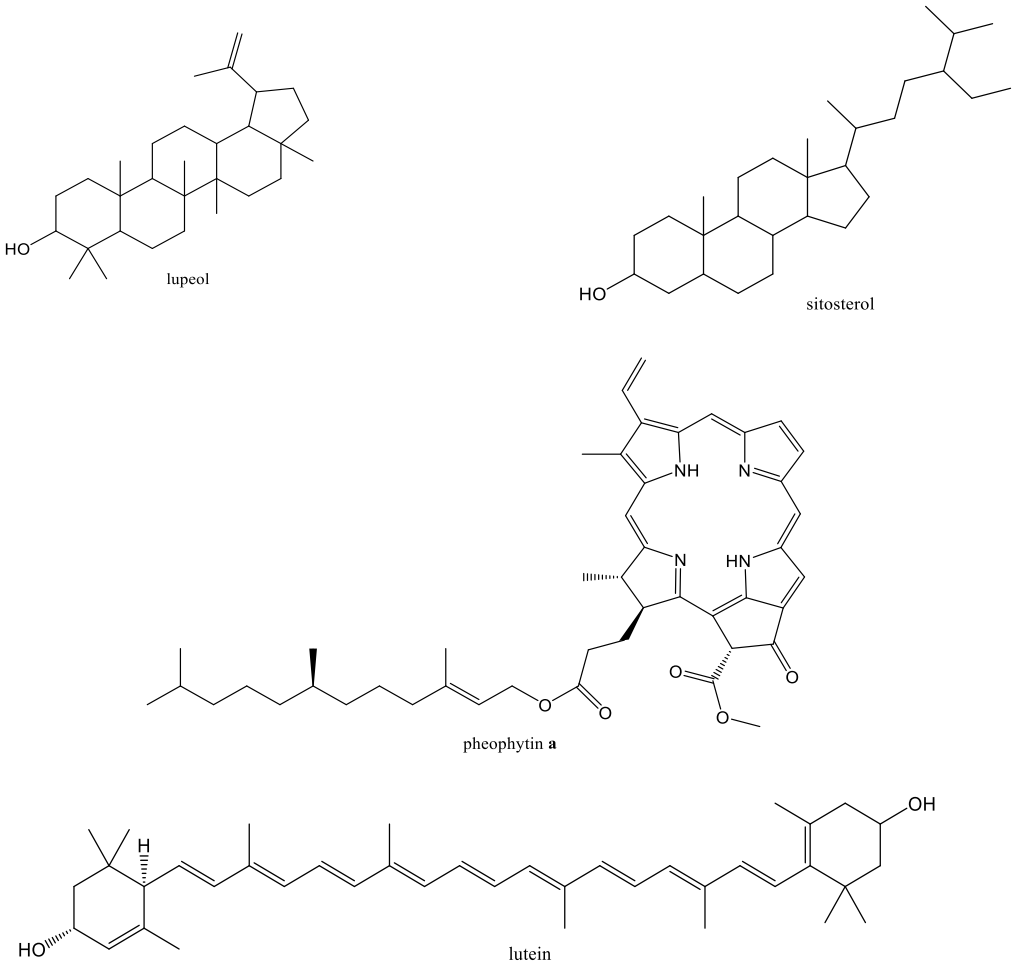
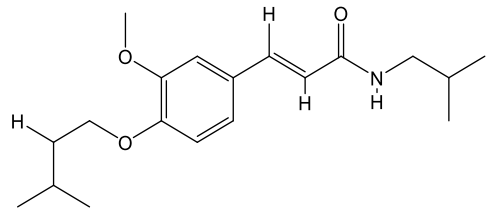
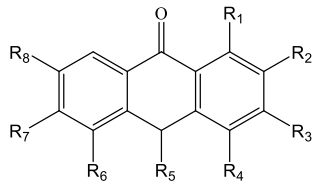


Figure S8. Anticancer and cytotocxic compounds isolated from *Zanthoxylum capense*



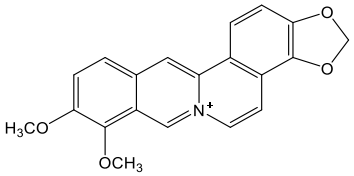
4-(isoprenyloxy)-3-methoxy-3,4-deoxymethylenedioxyfagaramide

Figure S9. Anticancer and cytotocxic compounds isolated from *Zanthoxylum chalybeum*

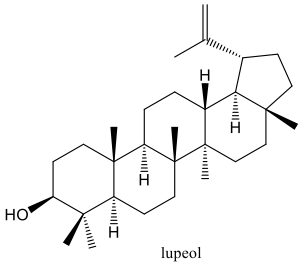


3-hydroxy-1-methoxy-10-methyl-9-acridone: R_1=OMe, R_2=H, R_3=OH, R_4=H, R_5=OMe, R_6=R_7=R_8=H
1-hydroxy-3-methoxy-10-methyl-9-acridone: R_1=OH, R_2=H, R_3=OMe, R_4=H, R_5=OMe, R_6=R_7=R_8=H
1-hydroxy-2,3-dimethoxy-10-methyl-9-acridone: R_1=OH, R_2=OMe, R_3=OMe, R_4=H, R_5=Me, R_6=R_7=R_8=H
1,3-dihydroxy-2-methoxy-10-methyl-9-acridone: R_1=OH, R_2=OMe, R_3= OH, R_4=H, R_5=Me, R_6=R_7=R_8=H
3-hydroxy-1,5,6-trimethoxy-9-acridone: R_1=OMe, R_2=R_4=R_5=R_8=H, R_3=OH, R_6=R_7=OMe, R_5=OMe, R_6=R_7=R_8=H

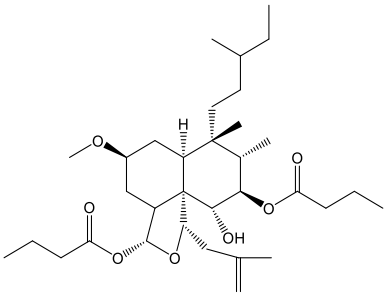
Figure S10. Anticancer and cytotocxic compounds isolated from *Zanthoxylum leprieurii*



berberine

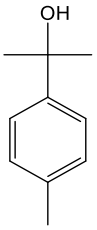


lupeol

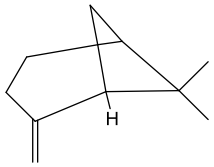


casearin G

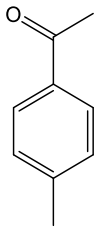
Figure S11. Anticancer and cytotocxic compounds isolated from *Zanthoxylum monophyllum*



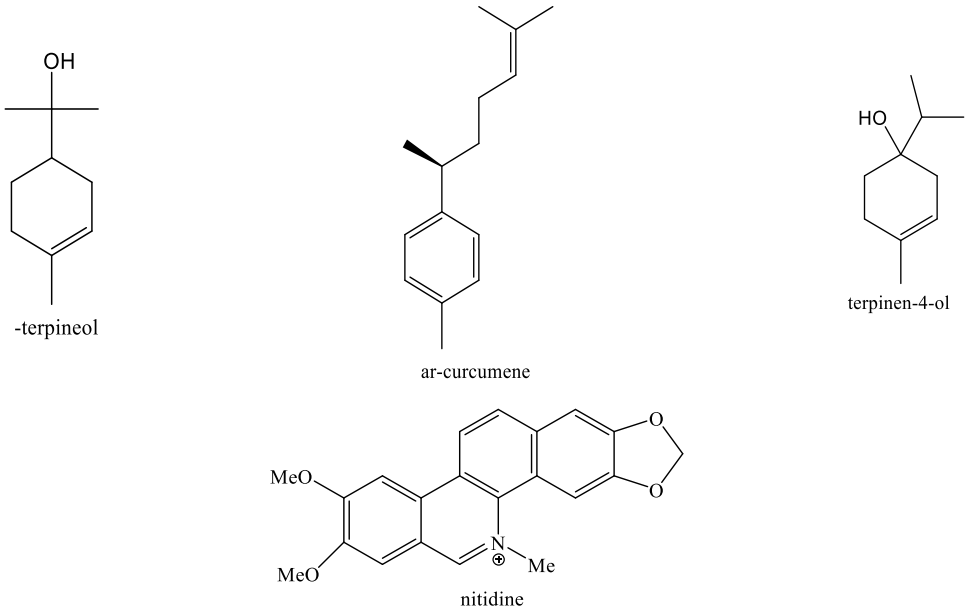
p-Cymen-8-ol



-Pinene



p-methyl-acetophenone



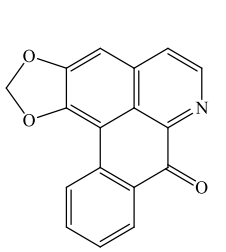
-terpineol

ar-curcumene

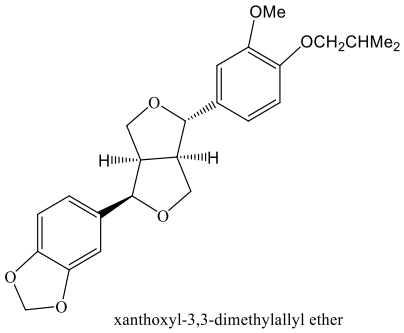
terpinen-4-ol

nitidine

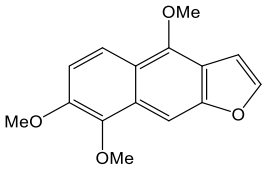
Figure S12. Anticancer and cytotocxic compounds isolated from *Zanthoxylum myriacanthum*



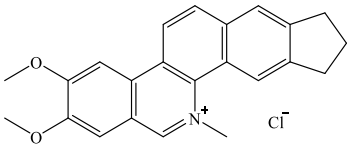
liriodenine



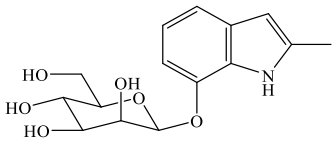
xanthoxyl-3,3-dimethylallyl ether



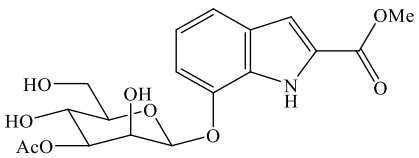
skimmianine



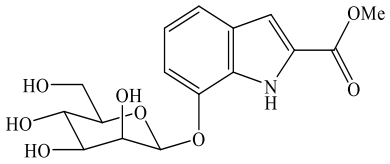
nitidine chloride



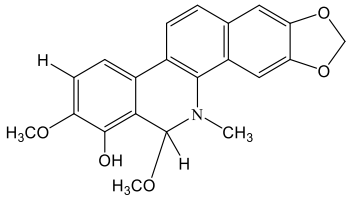
2-methyl-1H-indol-7-yl β-D-mannopyranoside



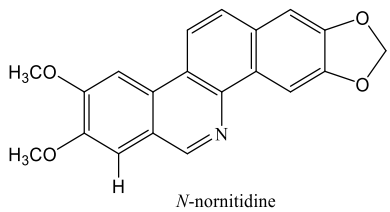
methyl 7-[(3-O-acetyl-β-D-mannopyranosyl)oxy]-1H-indole-2-carboxylate



methyl 7-(β-D-mannopyranosyloxy)-1H-indole-2-carboxylate



6-methoxy-7-hydroxydihydrochelerythrine: R_1 = H, R_2 = R_4 = OCH_3, R_3 = OH, R_5 = H
6-methoxydihydrochelerythrine: R_1 = H, R_2 = R_3 = R_4 = OCH_3, R_5 = H
8-(1′-hydroxyethyl)-7,8-dihydrochelerythrine: R_1 = H, R_2 = R_3 = OCH_3, R_4 = $CHOHCH_3$, R_5 = H



N-nornitidine

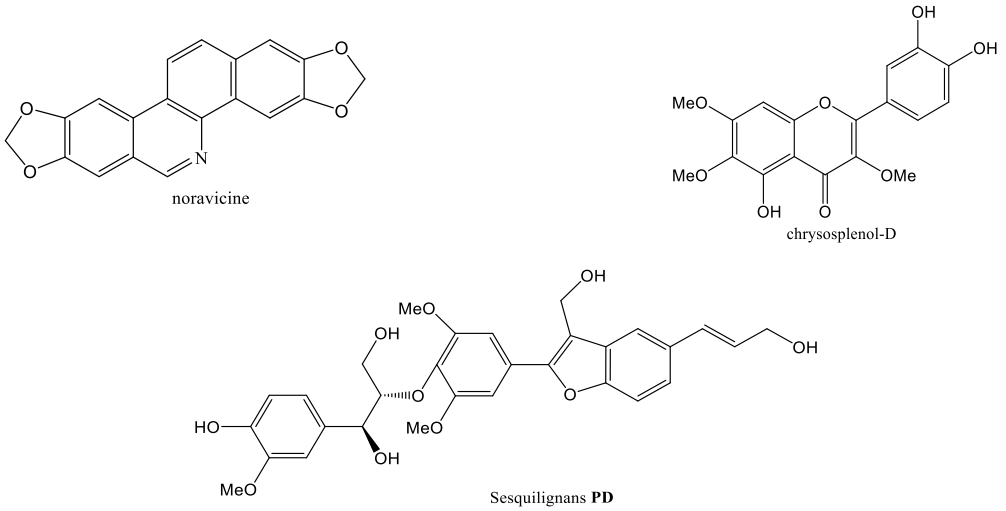
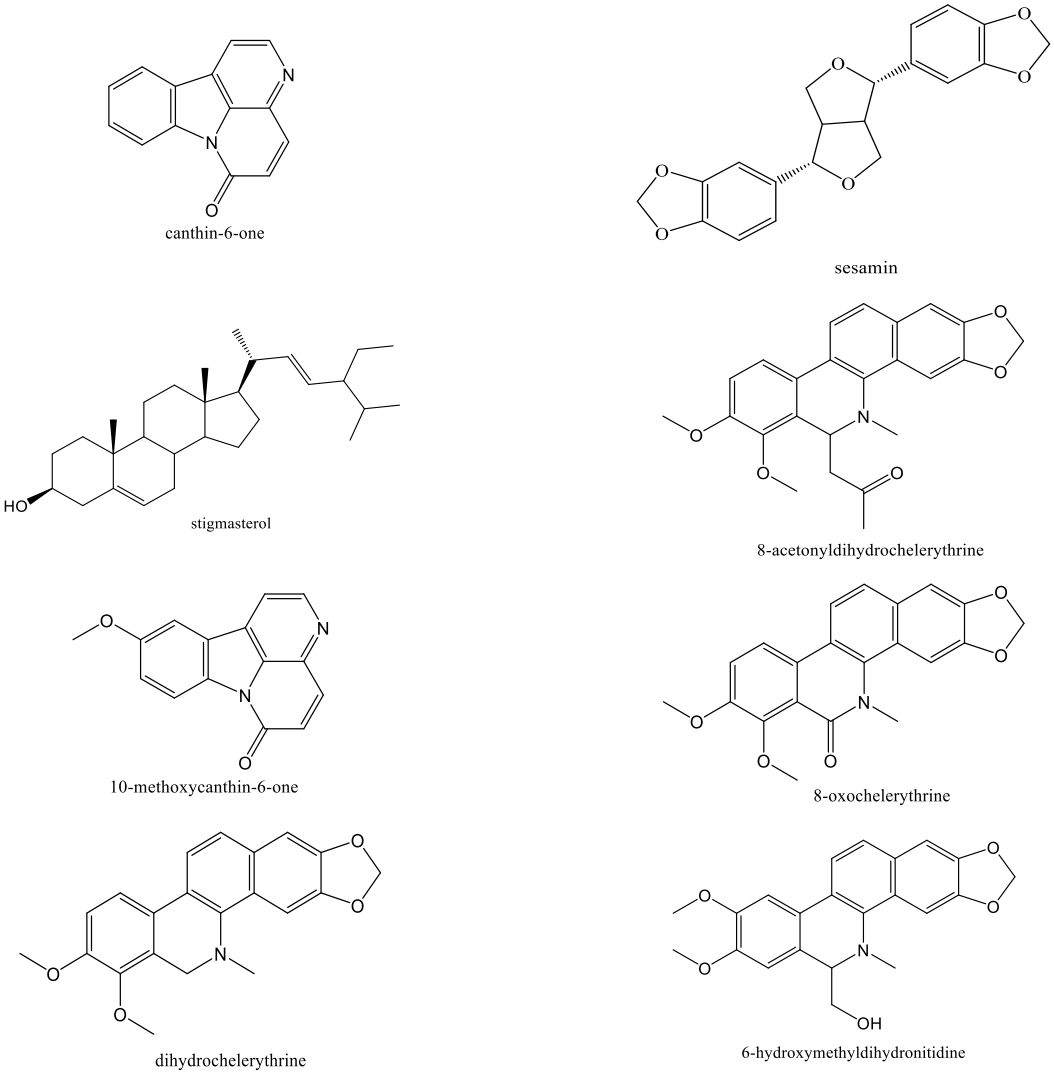
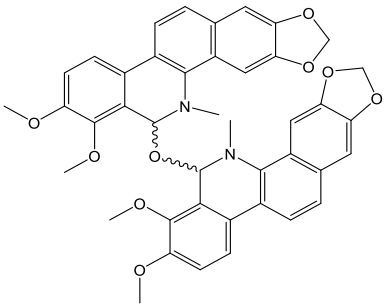


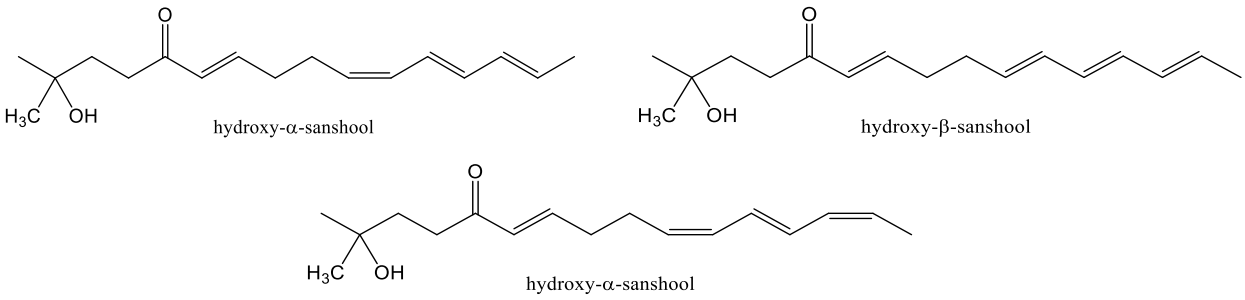
Figure S13. Anticancer and cytotocxic compounds isolated from *Zanthoxylum nitidum*





bis-[6-(5,6-dihydrochelerythrinyl)] ether

Figure S14. Anticancer and cytotocxic compounds isolated from *Zanthoxylum paracanthum*

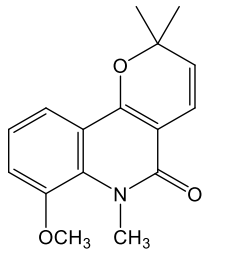


hydroxy-α-sanshool

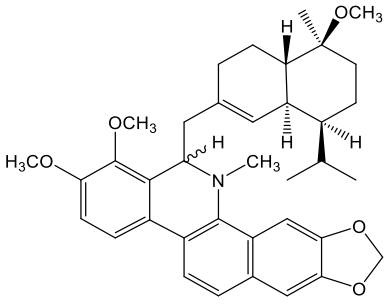
hydroxy-β-sanshool

hydroxy-α-sanshool

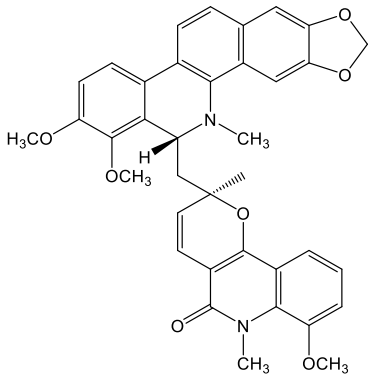
Figure S15. Anticancer and cytotocxic compounds isolated from Zanthoxylum piperitum



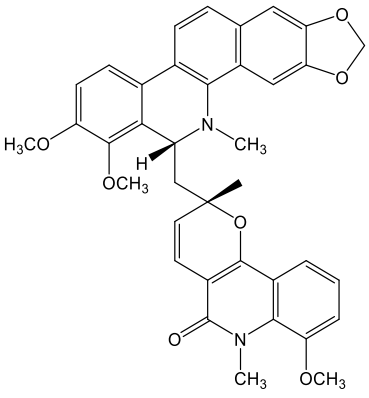
8-methoxy-N-methylflindersine



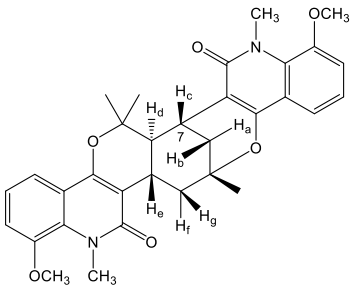
chelerybulgarine



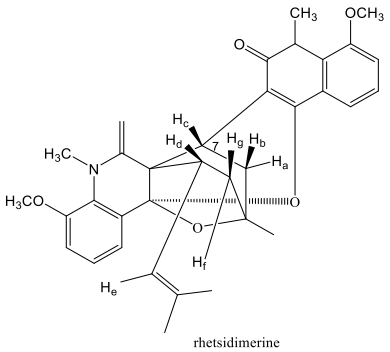
simulanoquinoline



2'-episimulanoquinoline



2,11-Didemethoxyvepridimerine B



rhetsidimerine

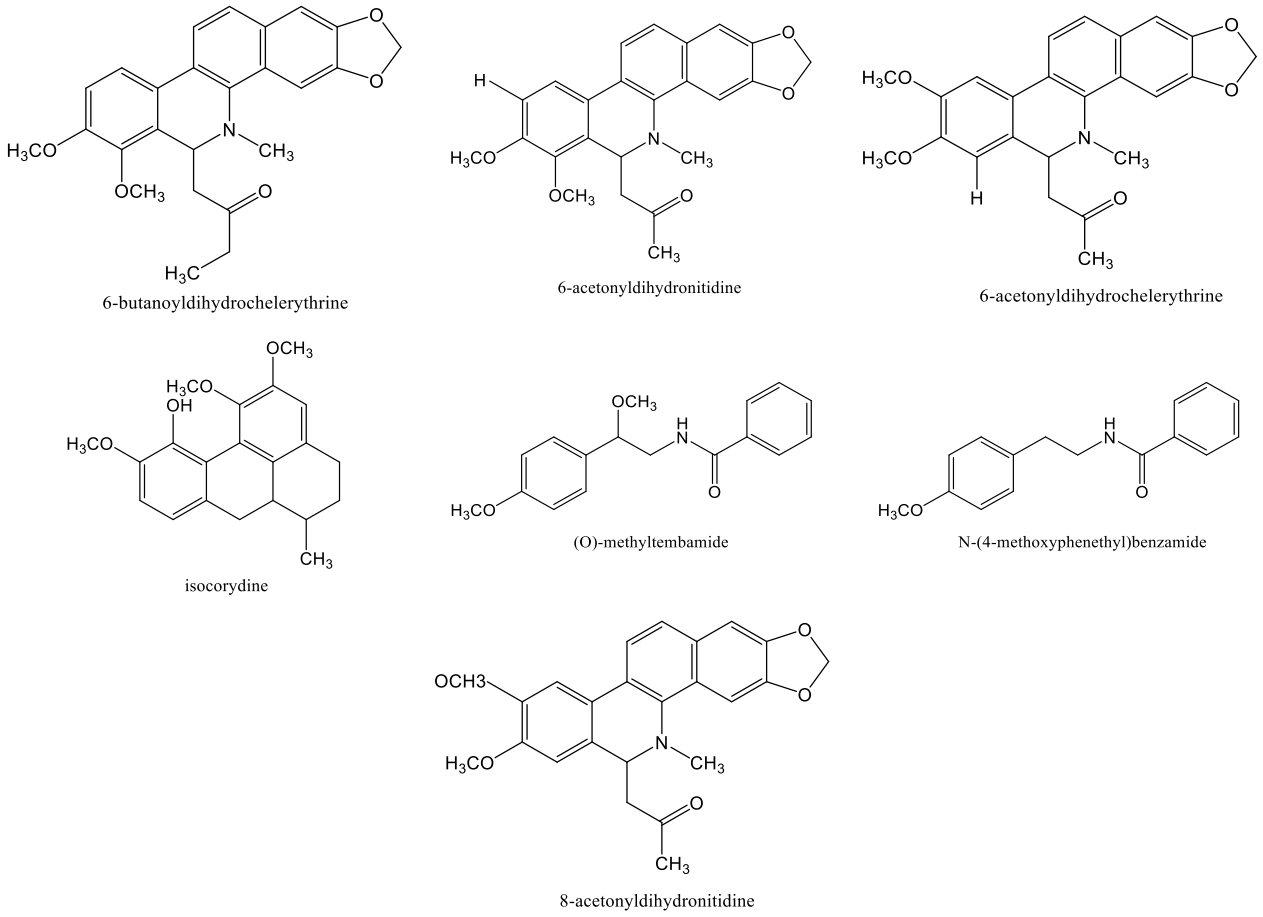
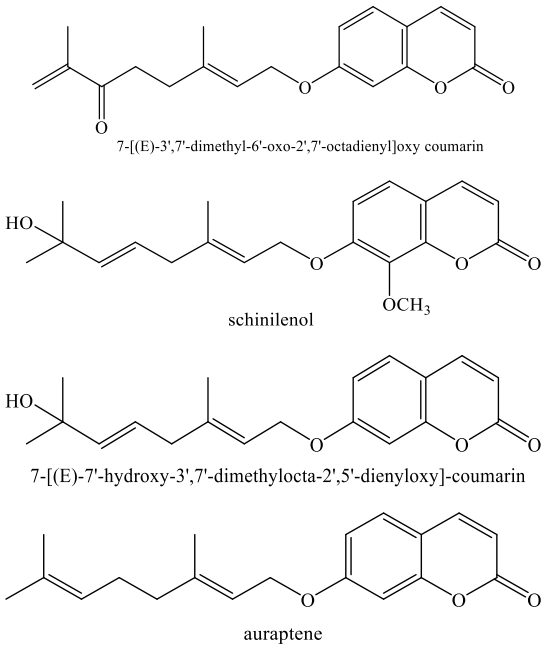
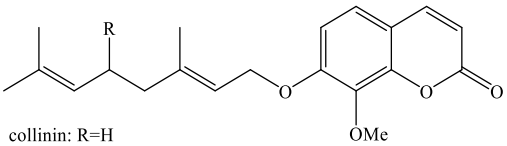
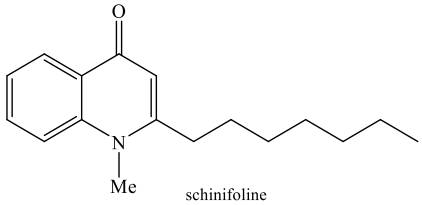


Figure S16. Anticancer and cytotocxic compounds isolated from Zanthoxylum rhesta



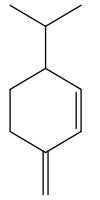


collinin: R=H
8-methoxyanisocoumarin H: R=OH
acetoxyschinifolin: R=OAc

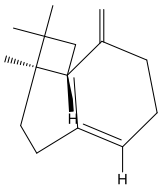


schinifoline

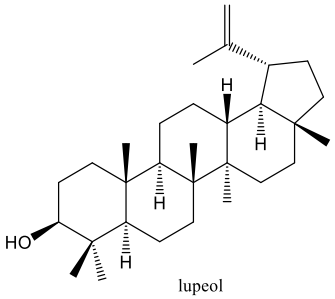
Figure S17. Anticancer and cytotocxic compounds isolated from *Zanthoxylum schinifolium*



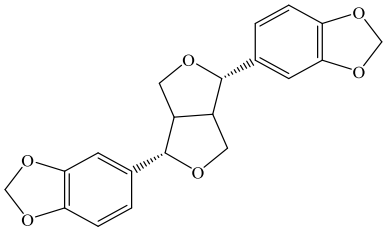
-phellandrene



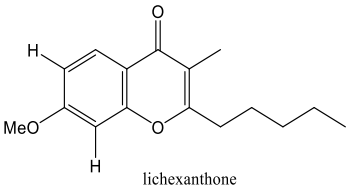
-caryophyllene



lupeol

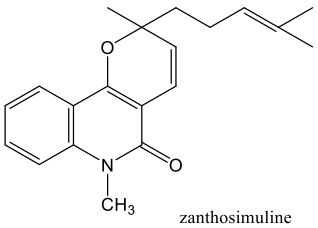


sesamin

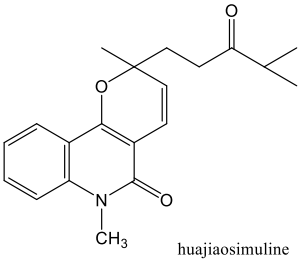


lichexanthone

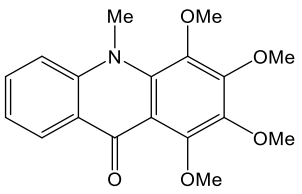
Figure S18. Anticancer and cytotocxic compounds isolated from *Zanthoxylum setulosum*



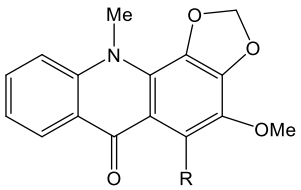
zanthosimuline



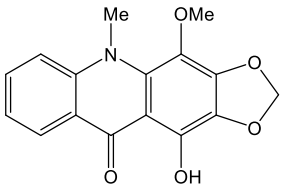
huajiaosimuline



melicopicine

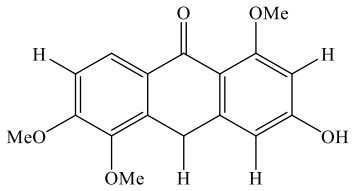


normelicopine: R = OH
melicopine: R = OMe

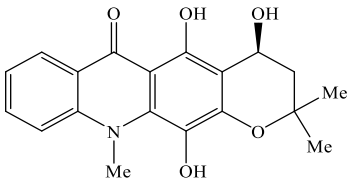


normelicopidine: R = OH
melicopidine: R = OMe

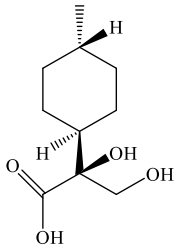
Figure S19. Anticancer and cytotocxic compounds isolated from *Zanthoxylum simulans*



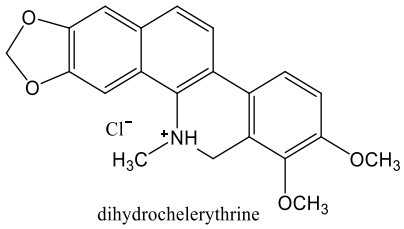
3-hydroxy-1,5,6-trimethoxy-9-acridone



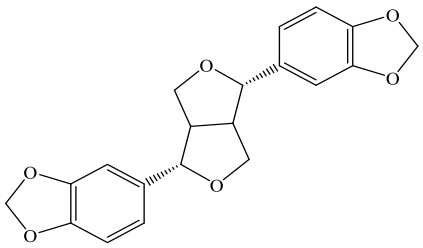
4-hydroxyzanthacridone



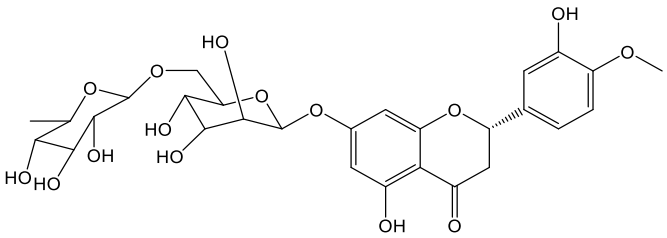
zantholic acid



dihydrochelerythrine

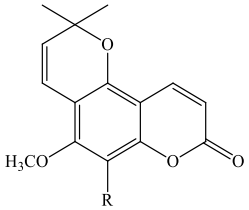


sesamin

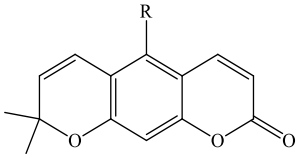


hesperidin

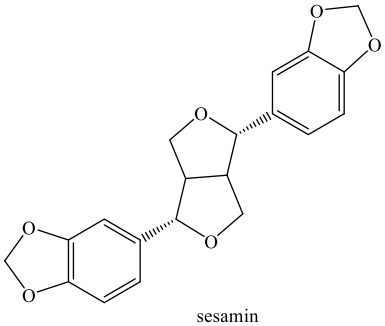
Figure S20. Anticancer and cytotocxic compounds isolated from *Zanthoxylum zanthoxyloides*



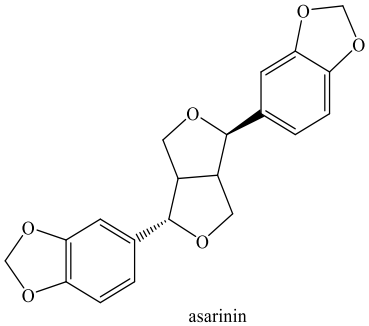
dipetalyne: R = isopentenyl
alloxanthoxyletin: R = H



xanthoxyletin: R = OCH_3
xanthyletin: R = H

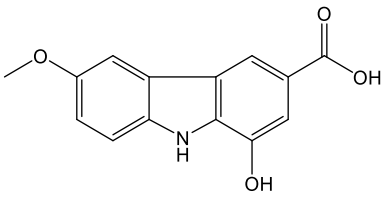


sesamin

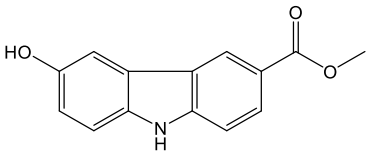


asarinin

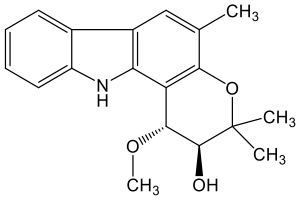
Figure S21. Anticancer and cytotocxic compounds isolated from *Zanthoxylum americanum*



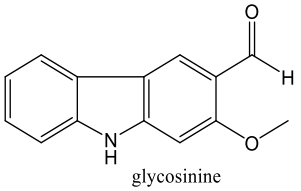
zanthoaustrones A



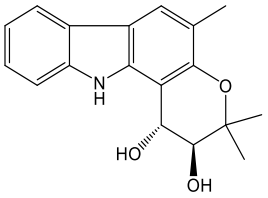
zanthoaustrones B



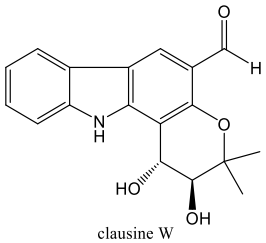
zanthoaustrones C



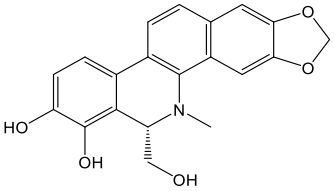
glycosinine



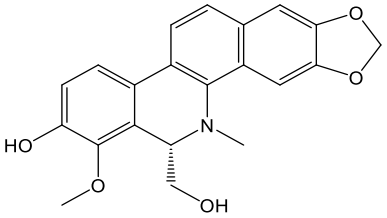
(-)-dihydroxygirinimbine



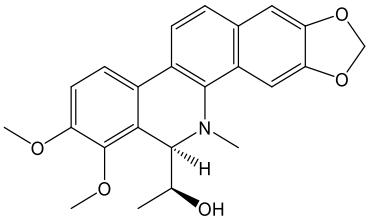
clausine W



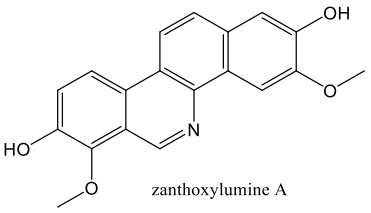
6-hydroxymethyl-7,8-demethylenedihydrochelerythrine



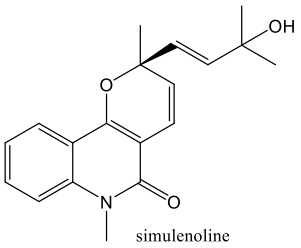
8*S*-10-*O*-de methylbocconoline



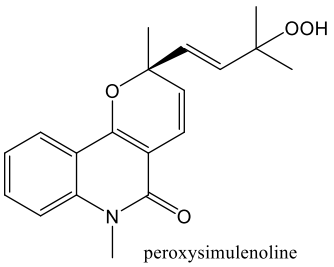
(10*S*,6*R*)-1-(dihydrochelerythrine-6-yl)ethanol



zanthoxylumine A

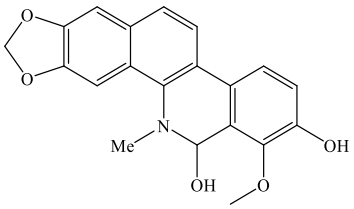


simulenoline

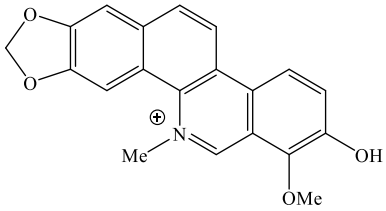


peroxysimulenoline

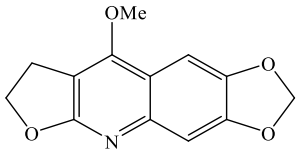
Figure S22. Anticancer and cytotocxic compounds isolated from *Zanthoxylum austrosinense*



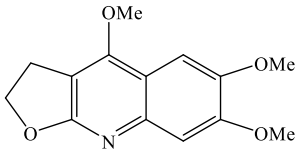
1-methoxy-12-methyl-12,13-dihydro-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]phenanthridine-2,13-diol



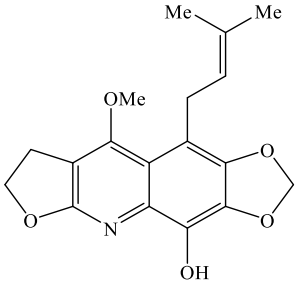
isofagaridine



maculine

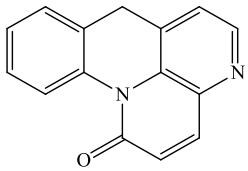


kokusaginine



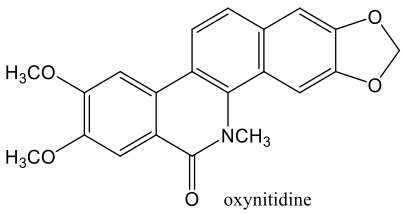
tecleaverdoornine

Figure S23. Anticancer and cytotocxic compounds isolated from *Zanthoxylum buesgenii*

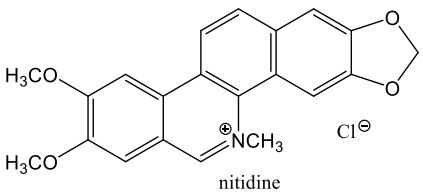


canthin-6-one

Figure S24. Anticancer and cytotocxic compounds isolated from *Zanthoxylum chiloperone*

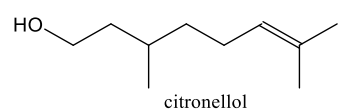


oxynitidine

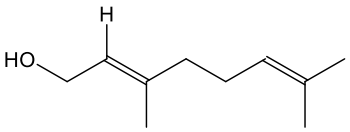


nitidine

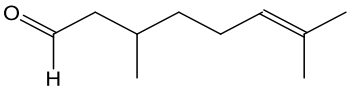
Figure S25. Anticancer and cytotocxic compounds isolated from Zanthoxylum coco



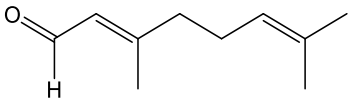
citronellol



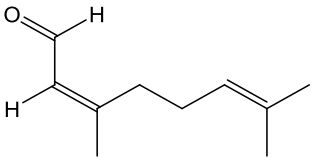
geraniol



citronellal

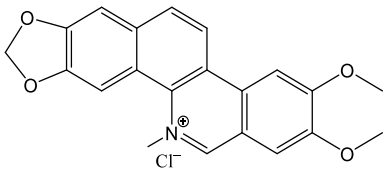


geranial

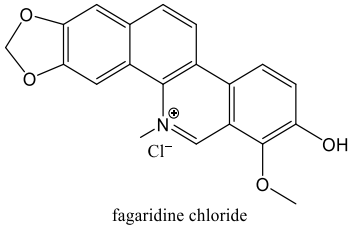


neral

Figure S26. Anticancer and cytotocxic compounds isolated from *Zanthoxylum fagara*

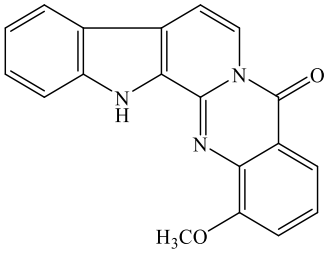


nitidine chloride

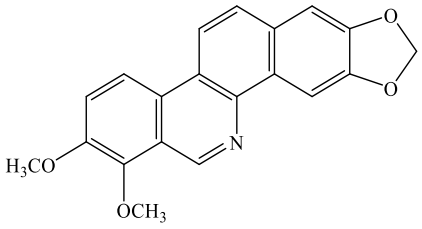


fagaridine chloride

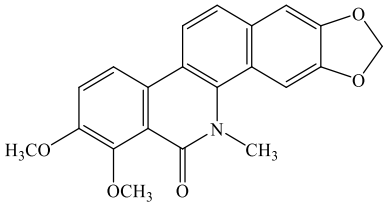
Figure S27. Anticancer and cytotocxic compounds isolated from *Zanthoxylum gilletii*



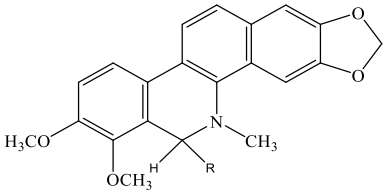
7,8-dehydro-1-methoxyrutaecarpine



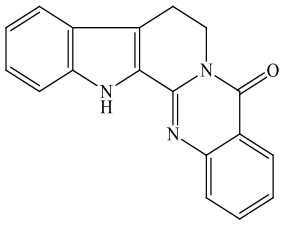
norchelerythrine



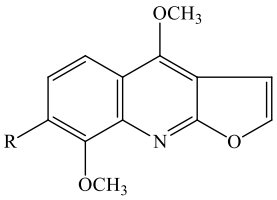
Oxychelerythrine



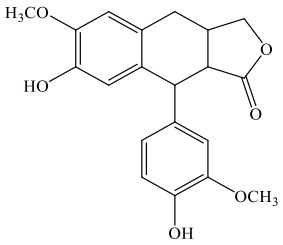
Dihydrocherythrinylacetaldehyde: R = CH_2CHO
6-acetonyldihydrochelerythrine: R = CH_2COCH_3



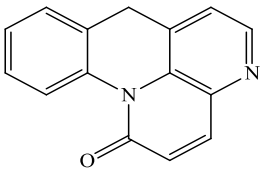
1-hydro- xyrutaecarpine



y-fagarine: R = H
skimmianine: R = OCH_3

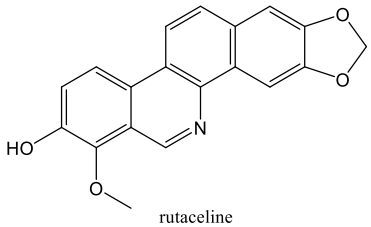


(-)-matairesinol



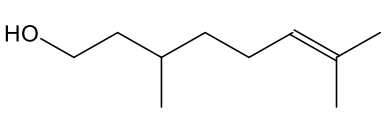
canthin-6-one

Figure S28. Anticancer and cytotocxic compounds isolated from *Zanthoxylum integrifoliolum*

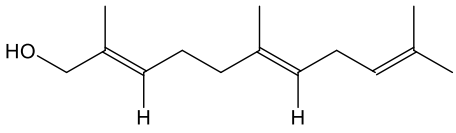


rutaceline

Figure S29. Anticancer and cytotocxic compounds isolated from *Zanthoxylum madagascariense*

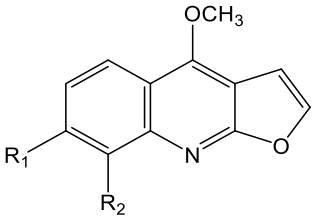


citronellol

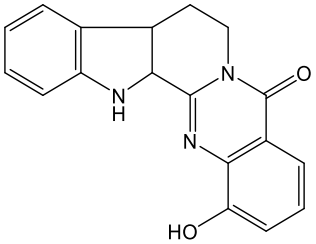


farnesol

Figure S30. Anticancer and cytotocxic compounds isolated from *Zanthoxylum monogynum*



γ-Fagarine: R_1=H, R_2=OCH_3
skimmianine: R_1=R_2=OCH_3
dictamnine: R_1=R_2=H



1-hydroxyrutaecarpine

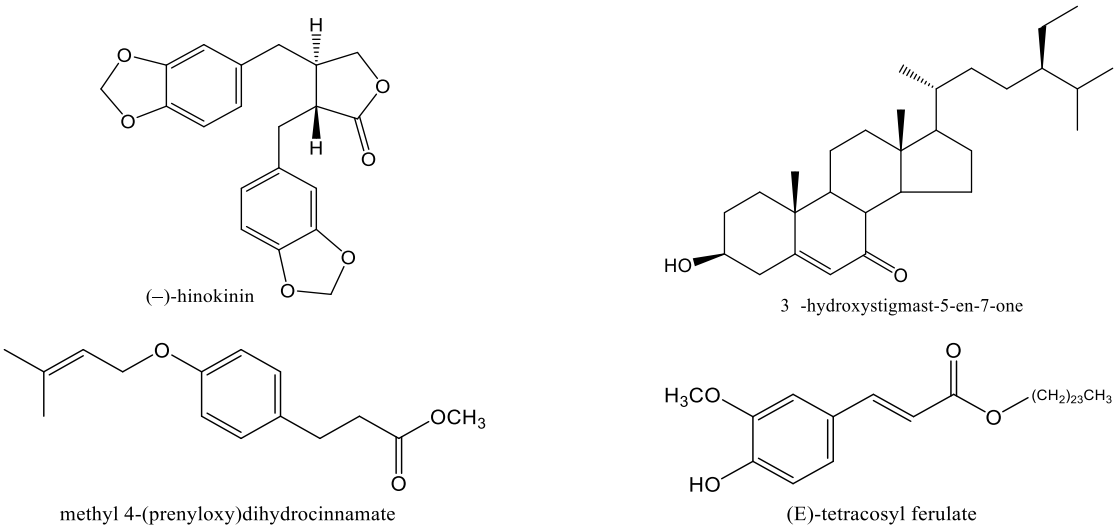


Figure S31. Anticancer and cytotocxic compounds isolated from *Zanthoxylum pistaciiflorum*

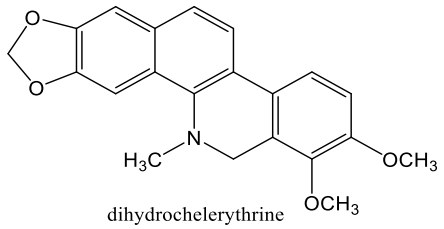


Figure S32. Anticancer and cytotocxic compounds isolated from *Zanthoxylum stelligerum*

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