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#### **REVIEW**



# A systematic review on black pepper (Piper nigrum L.): from folk uses to pharmacological applications

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#### **ABSTRACT**

Considered as the "King of spices", black pepper (Piper nigrum L.) is a widely used spice which adds flavor of its own to dishes, and also enhances the taste of other ingredients. Piper nigrum has also been extensively explored for its biological properties and its bioactive phyto-compounds. There is, however, no updated compilation of these available data to provide a complete profile of the medicinal aspects of P. nigrum. This study endeavors to systematically review scientific data on the traditional uses, phytochemical composition, and pharmacological properties of P. nigrum. Information was obtained using a combination of keywords via recognized electronic databases (e.g., Science Direct and Google Scholar). Google search was also used. Books and online materials were also considered, and the literature search was restricted to the English language. The country with the highest number of traditional reports of P. nigrum for both human and veterinary medicine was India, mostly for menstrual and ear-nose-throat disorders in human and gastrointestinal disorders in livestock. The seeds and fruits were mostly used, and the preferred mode of preparation was in powdered form, pills or tablets, and paste. Piper nigrum and its bioactive compounds were also found to possess important pharmacological properties. Antimicrobial activity was recorded against a wide range of pathogens via inhibition of biofilm, bacterial efflux pumps, bacterial swarming, and swimming motilities. Studies also reported its antioxidant effects against a series of reactive oxygen and nitrogen species including the scavenging of superoxide anion, hydrogen peroxide, nitric oxide, DPPH, ABTS, and reducing effect against ferric and molybdenum (VI). Improvement of antioxidant enzymes in vivo has also been reported. Piper nigrum also exhibited anticancer effect against a number of cell lines from breast, colon, cervical, and prostate through different mechanisms including cytotoxicity, apoptosis, autophagy, and interference with signaling pathways. Its antidiabetic property has also been confirmed in vivo as well as hypolipidemic activity as evidenced by decrease in the level of cholesterol, triglycerides, and low-density lipoprotein and increase in high-density lipoprotein. Piper nigrum also has anti-inflammatory, analgesic, anticonvulsant, and neuroprotective effects. The major bioactive compound identified in P. nigrum is piperine although other compounds are also present including piperic acid, piperlonguminine, pellitorine, piperolein B, piperamide, piperettine, and (-)-kusunokinin, which also showed biological potency. Most pharmacological studies were conducted in vitro (n = 60) while only 21 in vivo and 1 clinical trial were performed. Hence, more in vivo experiments using a pharmacokinetic and pharmacokinetic approach would be beneficial. As a conclusive remark, P. nigrum should not only be regarded as "King of spices" but can also be considered as part of the kingdom of medicinal agents, comprising a panoply of bioactive compounds with potential nutraceutical and pharmaceutical applications.

#### **KEYWORDS**

Black pepper; piperine; P. nigrum; spice; traditional medicine

# Introduction

Herbs and spices form an essential part of human nutrition since the dawn of humankind. They have been utilized for thousands of years to increase the flavor, color, and aroma of food, and are also recognized for their preservative characteristics and medicinal properties (Nagalingam and Arumugam 2015). Piper species belong to the Piperaceae family which is considered to be among the most ancient of

flowering plants growing in tropical regions, comprising of 13 genera (Scott et al. 2007). This diversified genus Piper includes 4,166 scientific plant names of species rank; of these 1,457 are accepted species names, 1,376 synonyms, and 1,333 unassessed (Durant-Archibold, Santana, and Gupta 2018).

Piper nigrum L., most commonly known as pepper, is considered to be the "king of spices" because of its massive trade share in the global market (Srinivasan 2007). The name "pepper" originates from the Sanskrit word pippali, which means berry (Kumar et al. 2011). Piper nigrum is a perennial woody aromatic climber that may grow to a height of 50-60 cm (Bui et al. 2017). White and black peppers are different in their time of harvest and processing techniques. White pepper is obtained by removing the pulp from ripe fruit, while the black pepper is produced by drying unripe fruit until a wrinkled formed; therefore, black pepper contains the pulp. Both white and black pepper has a wide range of applications, like spices, preservatives, insecticides, and also in herbal medicine (Wang et al. 2017).

Geographically, P. nigrum is mostly cultivated in hot and moist conditions (Ravindran and Kallupurackal 2012a). The primary areas of the black pepper cultivation are in the Western Ghats of the South Indian Peninsula, subsequently was introduced to other countries in South and Southeast Asia (Hao et al. 2012). Currently, Vietnam is the largest producer in the world, where black pepper is cultivated mainly in the southern region of Vietnam (Hao et al. 2012). In 2016, Vietnam led the world's top pepper producing countries (total production = 140,000 metric tonnes), followed by Indonesia (70,000 metric tonnes), India (48,500 metric tonnes), and Brazil (45,000 metric tonnes) (Ten, 2017). Pepper production in India has gradually decreased over the time since countries like Vietnam and Indonesia have started pepper cultivation (Hussain et al. 2017).

Piper nigrum is mainly used as a culinary item in a wide variety of dishes. In Western cuisine, black pepper is principally used as a seasoning ingredient to enhance food flavor as well as in food preserving (Ravindran and Kallupurackal 2012b). Whole peppercorns may be used in stews and soups or as part of a bouquet garni, together with parsley, thyme, and bay leaf. Lightly crushed peppercorns may be added to creamy sauces or to coat fillet steaks or chicken breasts to add some spiciness to the food. Ground white pepper is used in Thai and Chinese cuisine, in the preparation of salads, cream sauces, and light-colored sauces.

Apart from its culinary uses, the use of P. nigrum is well renowned in folk medicine in several countries. The biological profile of this plant is extensively studied by the scientific community, and a wealth of literature has emerged. There is, however, no updated compilation of these available data to provide a complete profile of the medicinal aspects of P. nigrum. In this context, this study aimed to systematically review scientific data on the traditional and pharmacological properties of P. nigrum

# Methodology

# Search strategy

Articles published from 1980 to 2018 were used for literature search using two key databases including Science Direct and Google Scholar. Google search was also used. Books and online materials were also considered. The literature search was restricted to only the English language. The scientific name of the plant was identified from The Plant List database (theplantlist.org). The chemical structures of the naturally occurring compounds previously identified in P. nigrum were drawn using the ChemDraw Professional v.17. 1 software.

The two following keywords "Piper nigrum", "black pepper" were combined with the following terms: "traditional", "medicinal", "ethnomedicinal", "ethnomedical", "ethnoveterinary", "pharmacological", and "phytochemical". The traditional uses of P. nigrum were obtained mainly from surveys previously carried out. To obtain a complete profile of the pharmacological properties of P. nigrum and not to miss any paper, a number of activities were screened using the following terms: "antioxidant", "antimicrobial", "antibacterial", "antifungal", "antidiabetic", "anticancer", "analgesic", "hypolipidemic" and so on.

#### Search results

In the search results (see Figure 1), 360 articles related to the search keywords were obtained on Science Direct and 430 articles on Google Scholar up to August 2018. Also, two sources from books were obtained. After the removal of duplicates, 359 articles were recovered from all three sources. When inclusion and exclusion criteria were applied, a total of 181 articles were included, of which 76 were on traditional uses, 24 on phytochemistry and 84 on pharmacological properties of P. nigrum. With regards to articles related to pharmacological properties, 37 were related to antimicrobial (in vitro = 37, in vivo = 0), 17 to antioxidant (in vitro = 13, in vivo = 4), 11 to anticancer (in vitro = 9, in vivo = 2), 5 to neuroprotective (in vitro = 0, in vivo = 5), 3 to anticonvulsant (clinical = 1, in vivo = 2) and hypoglycemic (in vitro = 1, in vivo = 2), and 2 articles on analgesic (in vitro = 0, in vivo = 2), hypolipidemic (in vitro = 0,  $in \ vivo = 2$ ) and anti-inflammatory ( $in \ vitro = 0$ , in vivo = 2).

#### Results and discussion

# Traditional uses of P. nigrum

Different parts (flower, seed, fruit, and leaf) of P. nigrum have been reported to treat or manage many ailments, as displayed in Table 1. Most reports on the traditional uses of P. nigrum have been reported in Asia. The country with the highest number of reports was India (n=42). This may be explained by the fact that India is one of the top producers of black pepper worldwide. Besides, Bangladesh (n=6) also reported some uses of P. nigrum in folk medicines. Other countries displayed low number of reports; Pakistan and Mexico (n=2), Cambodia, Thailand, Philippines, Malaysia, Poland, Mauritius, Algeria, and Morocco (n = 1). It is to be noted that although black pepper has been previously reported as an ingredient in European cuisine, there was only one reported use in traditional medicine from Poland.

Ethnomedicinal surveys documented so far revealed that the seeds were the most used part of P. nigrum (n = 45), followed by fruits (n=31) and leaves (n=8). However,

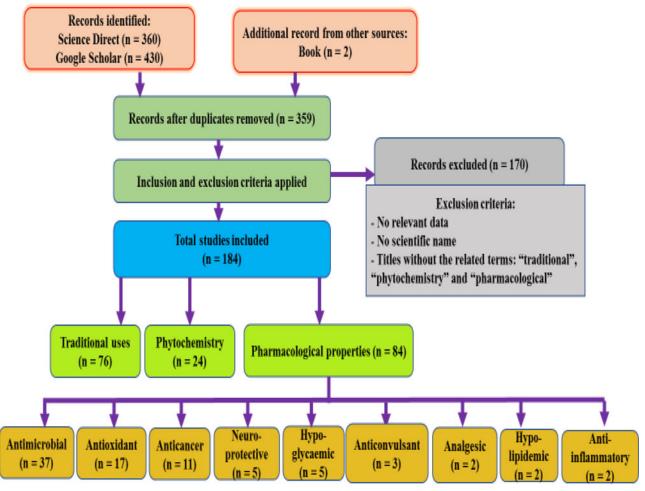


Figure 1. A visual representation of the selection process used in this review.

only two ethnomedicinal surveys reported the traditional use of P. nigrum flowers. In addition, diverse methods of preparations were used to target several diseases. The plant parts, mainly seeds and fruits, were ground to powder (n=40) and mixed with other plants either to form pills or tablets (n = 34). Other methods of preparations stated were as paste (n=23), crushed (n=8), boiled in milk (n=8), decoction (n=6), and infusion (n=4). Powdered form, pills or tablets, and paste were the most common methods of preparation reported since in these forms, they can be easily administered and stored. Another probable reason is that black pepper is used mainly as a spice in the diet, and therefore, it is mostly taken in its natural form in medicine as well.

Furthermore, among the diseases which P. nigrum were reported to treat (see Figure 2), menstrual disorders (n = 16) were mostly reported, which include menorrhagia, oligomenorrhea, hypomenorrhea, and dysmenorrhea. The next most reported treatment was for ear-nose-throat (ENT) related problems (n = 15), including a cough, sinusitis, throat pain, throat infection, and earache, followed by gastrointestinal disorders (n = 15) such as diarrhea and gastric problems. Piper nigrum was also used against skin diseases (n = 10), such as scabies, pruritus, bed sore, and boils, and also in the treatment of fever (n=9), jaundice (n=8), and snake bite (n=6).

# Ethnoveterinary uses of P. nigrum

It is important to highlight that P. nigrum was not only reported in the traditional medicine for human treatment but was also used in veterinary medicine to treat a range of ailments (see Table 2). Similar to the traditional human uses of P. nigrum, the highest number of ethnoveterinary reports were also from India (n = 10). The most reported plant parts of black pepper were seeds (n=29), followed by fruits (n=4), flowers (n = 1), and leaves (n = 1). The major methods of preparation reported were powder (n = 16), paste (n = 15), raw (n=3), boiled (n=1), and juice (n=1). On the other hand, three reports did not mention any methods of preparation and stated that they were given orally to the animals.

With regards to the targeted ailments in ethnoveterinary medicine, P. nigrum was mostly reported for use against gastrointestinal disorders (n = 19), including indigestion, bloating, diarrhea, flatulence, and stomach ache. Other uses outlined were in the treatment of cough and cold (n=5), skin diseases (n=3), loss of appetite (n=2), respiratory diseases (n = 2), and infertility (n = 2).

# Phytochemistry of P. nigrum

Several parts (fruit, seed, and root) of P. nigrum have been profiled, and more than 50 compounds have been identified

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Country	Part of plant used	Mode of preparation/ dosage	Ailments/Medicinal use	References
India	Seeds	N	Indigestion, body ache, bone fracture	Bhuyan and Baishya 2013
	Leaf Fruit	1 teaspoon of <i>P. nigrum</i> leaf juice and five to seven <i>P. nigrum</i> furity on the seven and the seven	Hypertension	Sethiya et al. 2018
	Seeds	Decortion	Respiratory system diseases	Venkatachalapathi et al. 2018
	Seed, flower, fruit	seeds of P. n	Snake bite	Upasani et al. 2017
		and orally consumed. The flower paste of <i>P. nigrum</i> is mixed with ghee and is orally given for 4 days.		
	Fruit	Maceration	Lactation Cough	Chander, Kartick, and Vijayachari 2015
	Fruit	Raw	Sinusitis, Vomiting	Vijayakumar et al. 2015
	IN See S	Powder Date	Stomach Problems	
	Seed		Aphthae, ulcer in intestine, crack	Bhat: Heade: and Heade 2012
			foot, cuts, gangrene, gingival wounds,	
			Otorrhoea, snake bite	
	ריטוד		Epilépsy	Sharma et al. 2013
	рөө	3–4 times per day till recovery. Seed nowder mixed with butter	Snake hite	Upadhyay et al 2010
	Seed	P. nigrum seeds are boiled in milk and water and taken	Malaria Splenomegaly	
		once every day in the early morning consecutively for 4 to 5 days.		
	Leaf	Leaves are crushed and applied topically applied on affected area of the skin.	Skin diseases	
	Leaf	Crushed leaves are mixed with mustard oil or cow milk or crushed with garlic bulbs and mixed with	Ringworm	
	Spag	Tingspora cordifolia plant paste and 5 seeds of <i>P. pionum</i>	s and my contract	
	מפפר	are orally consumed once per day in the morning	reducing the second sec	
	Fruit	Z	Throat pain Disease resistant Blood	Francis Xavier, Kannan, and
	Fruit	Z	circulation body simining Dandruff, pruritus, scabies, eczema, bed sore, boils	Auxilia 2013 Bhat et al. 2014
	Seed	Seed powder ground with equal amount of betel leaf paste is applied daily.	Eczema	Policepatel and Manikrao 2013
	Seed	A paste is prepared using 10g <i>Abutilon indicum</i> roots, 10g <i>Clerodendrum indicum</i> L. roots, 5 g <i>Cissampelos</i>	Headache	Dey et al. 2017
		pareira roots, 5 g Azadirachta indica leaves, 2 g Andrographis paniculata whole plant, 3 g fresh bulb of Curcuma longa, 15 g seeds of P. nigrum, 3 pieces Zingiber officinale and 3 pieces Polygala arvensis roots are made to pills. Two pills are taken per day; one in the early morning just before breakfast and another		
		at night.		
	Seed	10g <i>Laportea interrupta</i> roots and 10g <i>P. nigrum</i> seeds are ground to produce a powder. During epilepsy attack, a pinch of this powder is to be inhaled by	Epilepsy	
		the nationt for the next 4 days		

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Country	Part of plant used	Mode of preparation/ dosage	Ailments/Medicinal use	References
	Seed	50 g Gissus repanda stem, 25 g Leea macrophylla roots, 10 g Mucuna pruriens roots and 10 g P. nigrum seeds are ground and made to pills. Pills are taken on grouns and the good woods.	Epilepsy	
	Seed	Tinch of Dolichos lablab roots, Tinch Achyranthes aspera	Epilepsy	
		roots, 3-4 pieces <i>Moringa oleitera</i> dry flower, 7 pieces <i>P. nigrum</i> seeds and 1 g. Axis axis (horn dust) are are united to a north Dille of 1/2 inch		
		are ground and illiged to a passe. This or 1/3 inci- diameter ap repared from the paste. One pill is		
	Seed	S—10 pieces of <i>p. nigrum</i> seeds are grounded to dust and are mixed with 100 ml of hives fresh honey	Insomnia	
		(from Apis cerana indica) and applied inside the nose.		
	Seed	2g Axis axis dried skin, 5 mL Gallus gallus domesticus	Headache	
		blood, 1 piece <i>Spilostethus hospes</i> larva, 2 g <i>Hemidesmus indicus</i> roots and 5 <i>P. niarum</i> seeds are		
		mixed together to a paste. Pills, about the sizes of a		
		pea, are made from the paste. A pill is taken for 10 days		
	Seed	The leaves together with Zingiber officinale rhizome and	Reduce swelling	Jagtap, Deokule, and Bhosle 2006
		seeds of <i>P. nigrum</i> are decocted and is taken once every day for a period of 5 days.		
	Z	IN	Cardiovascular diseases	Esakkimuthu et al. 2016
	Ξ		Type 2 Diabetes	
	Fruit	Granulated leaves of P. nigrum fruits, Cynodon dactylon	Jaundice	Patel et al. 2011
		and <i>Phyllanthus amarus</i> are mixed to form an extract which is taken orally.		
	Z	Herbal medicine using <i>P. nigrum, A. vasica</i> and honey	Headache, earache, cold	Ayyanar and Ignacimuthu2011
	Z	Dy Karli Gaduciona nearers. Harbal madicina neina <i>Flottaria cardomomum 4 nal</i> -	Hoadacho asthma	
	<u> </u>	ango, P. nigrum, Zingiber officinale and sugar by Kani traditional healers.	ובמממבור מפנונות	
	Z	Herbal medicine using <i>Tephrosia purpurea, Carmona retusa, P. hymenophyllum</i> and <i>P. nigrum</i> by Kani trad-	Gastric problems	
		itional healers.		
	Fruit	Powder/Oral	Jaundice, Gastric problems, Indicestion	Sureshkumar, Silambarasan, and Avvanar 2017
	Seed	Same proportions of corm of Amorphophallus paeoniifo-	Haemorrhoids	Mallik, Panda, and Padhy 2012
		lius, roots of Rawolfia serpentina, dried rhizome of		
		Zingiber officinale, seeds of P. nigrum and P. longum are made into paste and tablets are prepared and		
		left to dry in the sun. Tablets are orally taken about 2 weeks		
	Seed	The endosperm of Caesalpinia bonduc L and seeds of P.	Fever	
		nigrum L. are crushed to a paste and is consumed together with honey.		
	Seed	A paste is made from 3 cm long root of Mimosa pudica	Haemorrhoids	
		L. with seeds of <i>P. nigrum</i> and mixed with curd. It is		
	Z	taken otany in empty stomach for 7 days. A powder is made from dried S <i>milax zevlanica</i> 1 roots	Infertility	
		along with P. Jongum and P. nigrum and is taken		
		orally twice daily.		

decoction is mixed with powrum and honey and on affected area.  on affected area.  ourpurea Pers. root is given with ract for one week.  ossocardia bosvallia is mixed er.  s arbor-tristis L. leaves are m seeds and made into tablets et is taken twice daily for are mixed with water and the daily.  m indicum seeds and 10 powrum and jaggery are boiled in it half the initial volume is halved are daily.  m indicum seeds and 10 powrum and jaggery are boiled in it half the initial volume is halved are daily.  In and fruits of Syzygium cumini ed orally for 2–3 days.  Ind to powder and are  on dactylon, Phyllanthus amarus ruits of P. nigrum and extracted. Stered.  on dactylon, Phyllanthus amarus ruits of P. nigrum and extracted.  seeds is taken orally.  seeds is taken orally.  seeds is taken orally.  tueous root extract (20 g in adendrum serratum (L.) Moon.  ch of powdered P. nigrum.  ch of powdered P. nigrum.  ch of powdered P. nigrum are  so of Cardiospermum halicacabum igrum.  ibum sativum and P. nigrum are  and the mixture is cooked with Bassica mirent is cooked with Bassica mirent is cooked with Bassica mirent is cooked with Bassica	(	rait of plaint used	Mode of preparation/ dosage	Ailments/Medicinal use	References
Fresh leaf pastes of <i>Clitotia tematea</i> L. with the paste of <i>P. nigum</i> is applied on affected area.  Decoction of <i>Tephrosia purpurea</i> Pers. root is given with the base of <i>P. nigum</i> extract for one week.  Dried leaf powder of <i>Cliosocardia bosvallia</i> is mixed with <i>P. nigum</i> powder.  Newly grown <i>Mycanthes arbor-trisis</i> I. Leaves are ground with <i>P. nigum</i> peeds and made into tablets of 2 g each. One tablet is taken twice daily for 14 days.  Seeds of <i>P. nigum</i> are ground along with leaves of <i>Punica granatum</i> and are mixed with water and the filtrate is taken twice of <i>Sesamum indicum</i> seeds and 10 powered seeds of <i>P. nigum</i> and ground seeds of <i>P. nigum</i> and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the due date of menses.  Two reaspoons of <i>Sesamum indicum</i> seeds are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the order of period.  Two teaspoons of <i>Sesamum indicum</i> seeds are boiled in vogether with <i>P. nigum</i> seeds and jaggery and taken or ally twice daily for five days before the onset of period.  A past is made using the roots of <i>Jylophora astima</i> -tica. The rapids orally.  Ground leaves of <i>Cynodon dactylon</i> , <i>Phyllanthus amarus</i> are mixed with the fruits of <i>P. nigum</i> and extracted. The extract is administered.  The tablets are made from a mixture of <i>Balanotis</i> roox-burgiii seeds, <i>P. nigum</i> and jaggery. The tablet is taken once daily for 3 days.  P. nigum seeds are made from a mixture of <i>Balanotis</i> roox-burgiiii seeds, <i>P. nigum</i> and jaggery. The tablet is taken once daily for 3 days.  P. nigum seeds are made from a mixture of <i>Balanotis</i> roox-burgiii seeds, <i>P. nigum</i> and jaggery. The tablet is taken once daily for 3 days.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of <i>Gleroderadum serratum</i> (L) Moon. are mixed with a pinch of powdered <i>P. nigum</i> .  Faren as vegetable		Seed		Cough	
Firsh leaf pastes of Clironia tennated L, with the paste of Pencition of Tephnosia purpues Pens. root is given with the 5g P, nigrum extract for one week.  Decoction of Tephnosia purpues Pens. root is given with the 5g P, nigrum extract for one week.  Developed the Toward of Glossocardia bosvallia is mixed with P, nigrum seeds and made into tablets of 2g each. One tablet is taken twice daily for 14 days.  Seeds of P, nigrum are ground along with leaves of Punica granatum and are mixed with water and the filtrate is taken twice per day for 15 days before the date of menses.  Two teaspoons of Sesamum indicum seeds and 10 powered seeds of P, nigrum and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the date of menses.  Two teaspoons of Sesamum indicum seeds are boiled together with P, nigrum seeds and jaggery are boiled together with P, nigrum seeds and jaggery and taken or ally twice daily for the days before the onset of period.  A past is made using the roots of Tylophora astimation of period.  A past is made using the roots of Tylophora astimation and is orally consumed orally for 2-3 days.  P, nigrum furits are ground to powder and are given orally.  Ground leaves of Gynoden dactylon, Phyllanthus amarus are mixed with the fruitis of P, nigrum and extracted. The extract is administered.  The extract is administered.  The extract is administered.  The tablets are made from a mixture of Balanotis tox-burghis each, P, nigrum and jaggery. The tablet is taken once daily for 3 days.  P, nigrum water of Grooden dactylon, Phyllanthus and mixer of Grooden dark of New and jaggery. The tablet is taken once daily for 3 days.  Penglum seeds are made from a mixture of Balanotis tox-burghis each, P, nigrum and jaggery the mixer of Cardiospermum halicacabum and leaf juice of P, nigrum.  Powder, decoction or aqueous root extract (20 gin 30 m. water) of Gerodendedm serrotum in powder of leaf and root bark of Newing ground and consumed.  Signilia solut			taken orally.		
Percention of Tephnosia purpured Pers. root is given with the 5 g P. nigrum extract for one week.  Direct leaf powder of of flossocardia bosvalia is mixed with P. nigrum powder.  Newly grown Myctanthes arbor-tristis L. leaves are ground with P. nigrum seeds and made into tablets of 2 g each. One tablet is taken twice daily for 14 days.  Seeds of P. nigrum are ground along with leaves of Punited ground un man man bare with early the punited ground and are mixed with water and the filtrate is taken twice daily.  Eight spoons of Sesamum indicum seeds and 10 powered of P. nigrum and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the due date of menses.  Two teaspoons of Sesamum indicum seeds and lopeweed of period.  A paste is made using the roots of Tylophora asthmorities. I won teaspoons of Sesamum indicum seeds are boiled together with P. nigrum seeds and jaggery and taken orally twice daily for five days before the onset of period.  A paste is made using the roots of Tylophora asthmorities or ally consumed orally for 12-3 days.  P. nigrum L., garlic and fruits of Syzgyium cuminian and is orally consumed orally for 2-3 days.  P. nigrum fruits are ground to powder and are given orally.  Ground leaves of Grondon dactylon, Phyllanthus amaus are mixed with the fruits of P. nigrum and jaggery. The tablet is taken one daily for 3-5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 ml water) of Clardodrafum serardum II.  Powder delation or aqueous root extract (20 g in 30 ml water) of Clardodrafum serardum II.  Powder of leaf and root bark of Kleinig grandiflora are mixed with the leaves of Cardiospermum halicacobum and leaf juice of P. nigrum and is cooked with Bossica oralls and seeds be and the series of Cardiospermum and the properties of P. nigrum and is cooked with Bossica oralls and seeds to the series of confidence or the series of the series and seeds be and the series of Car		Z	Fresh leaf pastes of Clitoria ternatea L. with the paste of	Swollen legs	Shanmugam, Rajendran, and
the 5 g. P. nigrum extract for one week.  Died leaf powder of folsosocadia bosvallia is mixed with P. nigrum powder.  Newly grown Mycranthes anbor-tristis L. leaves are ground with P. nigrum seeds and made into tablets of 2 g each. One tablet is taken twice daily for 14 days.  Seeds of P. nigrum and are mixed with water and the filtrate is taken twice paily.  Eight spoons of Sesamum indicum seeds and 10 powered used so P. nigrum and jaggery are boiled in water until t reaches half the initial volume is halved and is taken twice per day for 15 days before the due date of menses.  Two teaspoons of Sesamum indicum seeds are boiled together with P. nigrum seeds and jaggery and taken orgether with P. nigrum seeds and jaggery and taken orgether with P. nigrum seeds and jaggery and taken orgether with P. nigrum ground to 15 days before the onset of period.  A paste is made using the roots of Tylophora asthmatica, P. nigrum L. gadlic and fruits of Syzgyium cumini and is orally consumed orally for 2-3 days.  P. nigrum fuits are ground to powder and are given orally.  Ground leaves of Gynodon dactylon, Phyllanthus amarus are mixed with the fruits of P. nigrum and extractled. The tablets are made from a mixture of Balanotis roxburghii seeds, P. nigrum and jaggery. The tablet is taken once daily for 3-4 days.  P. nigrum seeds are made from a mixture of Balanotis from or 3-5 days.  Peccetion of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mt. water) of Clardobrumum sernatum (1) Moon.  Bet mixed with the leaves of Cardiospermum halicacobum and leaf juice of P. nigrum. Sooked with Bassica and seeds between the seeds between the second or sequebale.  Pheretting posthuman, Allium sativum and P. nigrum are gound and consumed.  Solum and leaf juice of P. nigrum.		Z	P. nigrum is applied on affected area. Decoction of <i>Tephrosia purpurea</i> Pers. root is given with	Urinary disorders	Suresn 2012
Dried leaf powder of Glossocardia bosvallia is mixed with P. nigrum powder.  Newly grown Wyctanthes arbo-tristis L. leaves are ground with P. nigrum seeds and made into tablets of 2 g each. One tablet is taken twice daily for 14 days.  Seeds of P. nigrum are ground along with leaves of Punica gronatum and are mixed with water and the filtrate is taken twice daily.  Eight spoons of Sesamum indicum seeds and 10 powered seeds of P. nigrum and jaggery are boiled in water until it reaches half the initial volume is halved and is taken write per day for 15 days before the due date of menses.  Two teaspoons of Sesamum indicum seeds are boiled together with P. nigrum seeds and jaggery and taken orally twice daily for five days before the onset of period.  A paste is made using the roots of Tylophora asthmatica, P. nigrum L., galfic and fruits of Syzguim cuminiand is orally consumed orally for 2-3 days.  P. nigrum fruits are ground to powder and are given orally.  Ground leaves of Cynodon dactylon, Phyllanthus amarus are mixed with the fruits of P. nigrum and extracted.  The extract is administered.  The tablets are made from a mixture of Balanotis roxburgin seeds, a nigrum and iaggery. The tablet is taken orally.  Fowder, decoction of aqueous root extract (20g in 30mL water) of Closodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum are mixed with a pinch of powdered P. nigrum are mixed with a pinch of powdered P. nigrum and leaf inte of P. nigrum. Powder of leaf and root bark of Kleinia grandiflora are mixed with a pinch of powdered P. nigrum are gound and consumed.  Sound and consumed.		:	the 5g <i>P. nigrum</i> extract for one week.		
Newton My grown My Wy Grown My Wy Grown My Wy My		₹	Dried leaf powder of Glossocardia bosvallia is mixed	Whooping cough	Wagh and Jain 2018
of 2 g each. One tablet is taken twice daily for 14 days.  Seeds of P. nigrum are ground along with leaves of Punica grandtum and are mixed with water and the filtrate is taken twice daily.  Seeds of P. nigrum and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the due date of menses.  Two teaspoons of Sesamum indicum seeds and 10 powered seeds of P. nigrum and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the orally twice daily for five days before the onset of period.  A paste is made using the roots of Tylophora asthmorita, paid in and is orally consumed orally for 2-3 days.  A nigrum fruits are ground to powder and are given orally.  A mand is orally consumed orally for 2-3 days.  P. nigrum fruits are ground from a mixture of Balanotis roxburdnis seeds, P. nigrum and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made from a mixture of Balanotis roxburdnis seeds, P. nigrum and jaggery. The tablet is taken once daily for 3-5 days.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of Grodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum.  Powder of leaf and root bank of Kleinig grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Powder of leaf and root bank of Kleinig grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum. Seed Millum Sativum and P. nigrum are gound and consumed.  Saland Sala		See	With <i>P. nigrum</i> powder. Newly grown <i>Nyctanthes arbor-trist</i> is I. Jeaves are	Memorragia	Bhatia et al 2015
Seeds of <i>P. nigrum</i> are ground along with leaves of <i>Punica granatum</i> and are mixed with water and the filtrate is taken twice daily.  Eight spoons of <i>Sesamum indicum</i> seeds and 10 powered seeds of <i>P. nigrum</i> and iaggery are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the due date of menses.  Two teaspoons of <i>Sesamum indicum</i> seeds are boiled together with <i>P. nigrum</i> seeds and jaggery and taken orally wice daily for five days before the onset of period.  A paste is made using the roots of <i>Tylophora asthmatica P. nigrum</i> L., garlic and fruits of <i>Syzygium cumini</i> and is orally consumed orally for 2–3 days.  P. nigrum fruits are ground to powder and are given orally.  Ground leaves of <i>Cynodon dactylon</i> , <i>Phyllanthus amaus</i> are mixed with the fruits of <i>P. nigrum</i> and extracted. The extract is administered.  The tablets are made from a mixture of <i>Balanotis rox-burghii</i> seeds, <i>P. nigrum</i> and jaggery. The tablet is taken orally.  Ground leaves of <i>Cynodon dactylon</i> , <i>Phyllanthus</i> amixed with ginger and honey. The mixture is orally administered for 3–5 days.  Perception of queeous root extract (20g in 30mL water) of <i>Clerodendrum serratum</i> (L.) Moon. are mixed with a pinch of powdered <i>P. nigrum</i> . Powder of leaves and seeds is taken orally.  Powder, decoction of eaves and seeds is taken orally.  Powder of leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Powder of leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Eaten as vegetable			of 2 g each. One tablet is taken twice daily for 14 days.	2.50	
filtrate is taken twice daily.  Eight spoons of <i>Sesamum</i> indicum seeds and 10 powered seeds of <i>P. niguum</i> and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice bail the initial volume is halved and is taken twice per day for 15 days before the due date of menses.  Two teaspoons of <i>Sesamum indicum</i> seeds are boiled together with <i>P. niguum</i> seeds and jaggery and taken orally wrice daily for five days before the onset of period.  A paste is made using the roots of <i>Tylophora asthmatica P. niguum</i> fuits are ground to powder and are given orally.  Ground leaves of <i>Cynodon dactylon</i> , <i>Phyllanthus amarus</i> are mixed with the fruits of <i>P. nigrum</i> and extracted. The extract is administered.  The tablets are made from a mixture of <i>Balanotis roxburghis</i> seeds, <i>P. nigrum</i> and jaggery. The tablet is taken orace daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3-5 days.  P. nigrum seeds are seed to powder and is mixed with ginger and honey. The mixture is orally administered for 3-5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20g in 30mL water) of <i>Clerodendrum serratum</i> (L.) Moon. are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Powder of leaf and root bark of <i>Kleinia grandiflora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Eaten as vegetable  Pheretima posthuman, Allium sativum and <i>P. nigrum</i> are gound and consumed.		Seed	Seeds of <i>P. nigrum</i> are ground along with leaves of	Leucorrhea	
Eight spoons of Sesamum indicum seeds and 10 powered seeds of <i>P. niguum</i> and jaggery are boiled in water until it reaches half the initial volume is halved and is taken wive per day for 15 days before the due date of menses.  Two teaspoons of Sesamum indicum seeds are boiled together with <i>P. nigrum</i> seeds and jaggery and taken orally twice daily for five days before the onset of paste is made using the roots of <i>Tylophora asthmatica</i> , <i>P. nigrum</i> L., garlic and fruits of <i>Syzygium cumini</i> and is orally consumed orally for 2–3 days. <i>P. nigrum</i> fruits are ground to powder and are given orally.  Ground leaves of <i>Cynodon dactylon</i> , <i>Phyllanthus amarus</i> are mixed with the fruits of <i>P. nigrum</i> and extracted. The extract is administered.  The tablets are made from a mixture of <i>Balanotis roxbughii</i> seeds, <i>P. nigrum</i> and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20g in 30mL water) of <i>Clerodendrum serratum</i> (1.) Moon. are mixed with a pinch of flowdered <i>P. nigrum</i> and leaf juice of <i>P. nigrum</i> .  Powder of leaf and root bark of <i>Kleinia grandiliora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Pheretima posthuman, Allium sativum and <i>P. nigrum</i> are gound and consumed.  Gallus gallis quented on the privature of privature and with Brassica sollus gallis gallis para proper privature and			Punica granatum and are mixed with water and the filtrate is taken twice daily.		
ered seeds of <i>P. nigrum</i> and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice. But the initial volume is halved due date of mense.  Two teaspoons of <i>Sesamum indicum</i> seeds are boiled together with <i>P. nigrum</i> seeds and jaggery and taken orally twice daily for five days before the onset of period.  A paste is made using the roots of <i>Tylophora asthmatica</i> , <i>P. nigrum</i> L., garlic and fruits of <i>Syzgium cumini</i> and is orally consumed orally for 2–3 days.  P. nigrum fruits are ground to powder and are given orally.  Ground leaves of <i>Cynodon dactylon</i> , <i>Phyllanthus amarus</i> are mixed with the fruits of <i>P. nigrum</i> and extracted. The extract is administered.  The tablets are made from a mixture of <i>Balamotis roxburghii</i> seeds, <i>P. nigrum</i> and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of <i>Clerodendrum serratum</i> (1.) Moon. are mixed with a pinch of powdered <i>P. nigrum</i> .  Powder (fleaf and root bank of <i>Klening grandiflora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Powder of leaf and coot bank of <i>Klening grandiflora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Pheretima posthuman, Allium sativum and <i>P. nigrum</i> are gound and consumed.  Gallus gallus domesticus meat is cooked with <i>Brassica gallus gallus domesticus</i> meat is cooked with <i>Brassica gallus gallus domesticus</i> meat is cooked with <i>Brassica gallus</i> domesticus neat is cooked with <i>Brassica gallus</i> domesticus meat is cooked with <i>Brassica gallus</i> domesticus meat is cooked with <i>Brassica gallus</i> domesticus meat is cooked with <i>Brassica gallus</i> domesticus means.		Seed	Eight spoons of Sesamum indicum seeds and 10 pow-	Oligomenorrhea	
Two teaspoons of <i>Sesamum indicum</i> seeds are boiled together with <i>P. nigrum</i> seeds and jaggery and taken orally twice daily for five days before the onset of period.  A paste is made using the roots of <i>Tylophora asthmatica</i> , <i>P. nigrum</i> L, galic and fruits of <i>Syzgium cumini</i> and is orally consumed orally for 2–3 days. <i>P. nigrum</i> fruits are ground to powder and are given orally.  Ground leaves of <i>Cynodon dactylon</i> , <i>Phyllanthus amarus</i> are mixed with the fruits of <i>P. nigrum</i> and extracted. The extract is administered. The tablets are made from a mixture of <i>Balanotis roxburghii</i> seeds, <i>P. nigrum</i> and jaggery. The tablet is taken once daily for 3 days. <i>P. nigrum</i> seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20g in 30 mL water) of <i>Clerodendrum serratum</i> (L.) Moon. are mixed with a pinch of powdered <i>P. nigrum</i> . Powder of leaf and root bark of <i>Kleinia grandiflora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Eaten as vegetable <i>Pheretima posthuman</i> , <i>Allium sativum</i> and <i>P. nigrum</i> are gound and consumed. <i>Gallus gallus domesticus</i> meat is cooked with <i>Bassica prisca alius alius alius and prisca superium and alius alius alius and alius ali</i>			ered seeds of <i>P. nigrum</i> and jaggery are boiled in water until it reaches half the initial volume is halved and is taken twice per day for 15 days before the due date of menses.		
together with P. niguum seeds and jaggery and taken orally twice daily for five days before the onset of period.  A paste is made using the roots of Tylophora asthmatica, P. nigrum L., garlic and fruits of Syzgium cumini and is orally consumed orally for 2–3 days.  P. nigrum fruits are ground to powder and are given orally.  Ground leaves of Cynodon dactylon, Phyllanthus amarus are mixed with the fruits of P. nigrum and extracted. The extract is administered.  The extract is administered.  The tablets are made from a mixture of Balanotis roxburghii seeds, P. nigrum and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum.  Powder of leaf and root bark of Kleinia grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Bassica prive a diversal price of P. nigrum and prive a diversal prive of P. nigrum and prive and prive and prive and a diversal pr		Seed	Two teaspoons of Sesamum indicum seeds are boiled	Hypomenorrhea	
A paste is made using the roots of Tylophora asthmatica, P. nigrum L., garlic and fruits of Syzygium cuminiand is orally consumed orally for 2–3 days.  P. nigrum fruits are ground to powder and are given orally.  Ground leaves of Cynodon dactylon, Phyllanthus amarus are mixed with the fruits of P. nigrum and extracted. The extract is administered.  The extract is administered.  The tablets are made from a mixture of Balanotis roxburghii seeds, P. nigrum and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum.  Powder of leaf and root bark of Kleinia grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica is a dillus domesticus meat is cooked with Brassica dillus domesticus meat is cooked with Brassica			together with <i>P. nigrum</i> seeds and jaggery and taken orally twice daily for five days before the onset of period.	:	
ities, principle of special properties, and fruits of Syzygium cuminiand is orally consumed orally for 2–3 days.  P. nigrum fruits are ground to powder and are given orally.  Ground leaves of Cynodon dactylon, Phyllanthus amarus are mixed with the fruits of P. nigrum and extracted.  The extract is administered.  The tablets are made from a mixture of Balanotis roxburghii seeds, P. nigrum and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20g in 30mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum.  Powder of leaf and root bark of Kleinia grandiflora are mixed with he leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica signing Allium Sativum and Sallus sallus domesticus meat is cooked with Brassica signing Allium Sativum and Sallus s		Z	A paste is made using the roots of T <i>vlophorg asthma</i> -	laundice	Sharma et al. 2012
P. nigrum fruits are ground to powder and are given orally.  Ground leaves of Cynodon dactylon, Phyllanthus amarus are mixed with the fruits of P. nigrum and extracted. The extract is administered.  The extract is administered.  The tablets are made from a mixture of Balanotis roxburghii seeds, P. nigrum and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum. Powder of leaf and root bark of Kleinia grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica signilus domesticus meat is cooked with Brassica dillus administracia posthuman, Allium sativum and perional programa and perional programa and perional programa and perional programa is cooked with Brassica signilus domesticus meat is cooked with Brassica		Ξ	tica, P. nigrum L., garlic and fruits of Syzygium cumini and is orally consumed orally for 2–3 days.		100
Ground leaves of Cynodon dactylon, Phyllanthus amarus are mixed with the fruits of P. nigrum and extracted. The extract is administered.  The extract is administered.  The tablets are made from a mixture of Balanotis roxburghii seeds, P. nigrum and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum.  Powder of leaf and root bark of Kleinia grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica signally admission and sulfirm and believed to the program and believed to the		Fruit	P. nigrum fruits are ground to powder and are given orally.	Jaundice	
are mixed with the fruits of <i>P. nigrum</i> and extracted. The extract is administered.  The extract is administered.  The tablets are made from a mixture of <i>Balanotis roxburghii</i> seeds, <i>P. nigrum</i> and jaggery. The tablet is taken once daily for 3 days. <i>P. nigrum</i> seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of <i>Clerodendrum serratum</i> (L.) Moon. are mixed with a pinch of powdered <i>P. nigrum</i> .  Powder of leaf and root bark of <i>Kleinia grandiflora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Eaten as vegetable  Pheretima posthuman, Allium sativum and <i>P. nigrum</i> are gound and consumed.  Gallus gallus domesticus meat is cooked with <i>Brassica</i> signally administration meat is cooked with <i>Brassica</i>		Fruit	Ground leaves of Cynodon dactylon, Phyllanthus amarus	Jaundice	
The tablets are made from a mixture of <i>Balanotis roxburghii</i> seeds, <i>P. nigrum</i> and jaggery. The tablet is taken once daily for 3 days. <i>P. nigrum</i> seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of <i>Clerodendrum serratum</i> (L.) Moon. are mixed with a pinch of powdered <i>P. nigrum</i> . Powder of leaf and root bark of <i>Kleinia grandiflora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> .  Eaten as vegetable  Pheretima posthuman, Allium sativum and <i>P. nigrum</i> are gound and consumed.  Gallus gallus domesticus meat is cooked with <i>Brassica pinca Allium and Allium sativum</i> in second of the second of			are mixed with the fruits of <i>P. nigrum</i> and extracted. The extract is administered.		
burghii seeds, P. nigrum and jaggery. The tablet is taken once daily for 3 days.  P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum. Powder of leaf and root bark of Kleinia grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica is a dillus domesticus meat is cooked with Brassica dillus domesticus meat is cooked with Brassica		Z	The tablets are made from a mixture of Balanotis rox-	Jaundice	
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for 3–5 days.  Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 gin 30 mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum.  Powder of leaf and root bark of Kleinia grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus adults domesticus meat is cooked with Brassica in a single of the statement of the same of the same is a cooked with brassical and consumed.		Seed	P. nigrum seeds are made to powder and is mixed with ginger and honey. The mixture is orally administered	Common cold	Lingaraju, Sudarshana, and Rajashekar 2013
Decoction of leaves and seeds is taken orally.  Powder, decoction or aqueous root extract (20 g in 30 mL water) of Clerodendrum serratum (L.) Moon. are mixed with a pinch of powdered P. nigrum.  Powder of leaf and root bark of Kleinia grandiflora are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica in a single Allium and D. nigrum and D. nigrum and D. nigrum are gallus admesticus meat is cooked with Brassica and Allium and D. nigrum			for 3–5 days.		
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are mixed with a pinch of powdered <i>P. nigrum</i> . Powder of leaf and root bark of <i>Kleinia grandiflora</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf juice of <i>P. nigrum</i> . Eaten as vegetable Pheretima posthuman, Allium sativum and <i>P. nigrum</i> are gound and consumed.  Gallus dollus donesticus meat is cooked with <i>Brassica</i>		Z	Powder, decoction or aqueous root extract (20 g in 30 mL water) of <i>Gerodendrum serratum</i> (L.) Moon.	Fever	Patel, Acharya, and Acharya 2014
Provider of teal and toot bank of nemial granding are mixed with the leaves of Cardiospermum halicacabum and leaf juice of P. nigrum.  Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus donesticus meat is cooked with Brassica price and Allium Card D. price and D. price and D. price and Allium Card D. price and D. price an		<b>3</b> ****	are mixed with a pinch of powdered <i>P. nigrum.</i>	استراطويم وأعلمون	And the second of the second
Eaten as vegetable  Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica prince of the statement of		רבמו	rowuer of lea and toot bark of <i>nemua grandinou</i> are mixed with the leaves of <i>Cardiospermum halicacabum</i> and leaf uice of <i>P. niarum</i> .	dasure problems	Ayyanal anu ignaciinunu 200
Pheretima posthuman, Allium sativum and P. nigrum are gound and consumed.  Gallus gallus domesticus meat is cooked with Brassica		Fruit	Eaten as vegetable	Increases breast milk as well as relieves pain after child birth	Buragohain 2008
gound and consumed.  Gallus galus domesticus meat is cooked with Brassica  pion Allium ona D inform and Allium catium in		Z	Pheretima posthuman, Allium sativum and P. nigrum are	Lactogogue	Chellappandian et al. 2014
Contrar delines contrar and a		Z	gound and consumed. Gallus gallus domesticus meat is cooked with <i>Rrassica</i>	Stomarharhe	
		Ē	nigra, Allium cepa, P. nigrum and Allium sativum in		

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Part of plant used  Note that control of disease and control disease  Note that the disease of the provider and consumed only.  Seed On the disease of the provider and disturbination and fallow astrony and the second of place of fresh not of the provider and disturbination and fallow astrony and seed are seed the profit of the profit of the seed	ומחוב וי כסוותוותבת.				
A parameter of the seek of the	Country	Part of plant used	Mode of preparation/ dosage	Ailments/Medicinal use	References
Cough, bronchits  Provided Seasor of the form promoted Allum softwar and season of the contract and an		Seed	P. nigrum seeds are soaked in pig bile, allowed to air	Fever	
Cough, bornchias  Powdeed Becar of dis primipenus transment and Mann strawm mixed with C forgam and Allam strawm mixed with C forgam and Allam strawm and is construed becare of dispersion to the Steam and Allam strawm and is construed because the steam and the steam of the stea		Z	Gallus gallus domesticus meat is mixed with Brassica nigra, Allium cepa, P. nigrum and Allium sativum and	Jaundice	
One tesspoon of juice of fresh sem half of Bombox  Agorngus coremous Wild., seed a tesspoon of juice of fresh root of  Agorngus coremous Wild., seed are ground to powder  and act as aphrodisac.  10g finds or of Eephantopus scaler. Librag with 21  10g finds or of Eephantopus scaler. Librag with 21  10g finds or of Eephantopus scaler. Librag with 21  10g finds or of Eephantopus scaler. Librag with 22  10g finds or of Eephantopus scaler. Librag with seven or two Adonglera build or 1 Levens a agound to powder  10g finds or of the Adonglera build or Levens a ground to powder  10g finds or standard with contract and many stomes and many stomes and spannership and or two Adonglera build or 1 Levens and or 1 Levens and 1 Levens and or 1 Levens and 1 Levens		N	cooked in urine and consumed. Powdered Bezoar of <i>Bos primigenius taurus</i> Linnaeus is mixed with <i>P. Iongum, P. nigrum</i> and <i>Allium sativum</i>	Cough, bronchitis	
cibit Lore tespoon of the control of captures and the captures are captured entities and the captures are captured and cap		Cood	and is consumed orally.	Contractions important contractor	Rohors and Mirrs 2005
A favorages recursors with a set as the condition of processed suggested to another in empty stomach to working the condition of processed suggested to another in empty stomach to make the condition of processed suggested and taken on of by the condition of processed suggested and taken of the condition of the		מפטר	ceiba L, one teaspoon of juice of fresh root of	rhea, sterility, nocturnal emission,	Delicia alla Misia 2003
10 files to or of Expendencians cancer Leave she good and taken only in empty stomach two interest daily for some formations useder. Leave she good and taken onally the special power of the Prington. Lised see good and taken onally the prington of the Prington. Lised see good and taken onally the Prington of the Prington. Lised see good and taken onally the Prington of the Pringt			Asparagus racemosus Willd., seven dried seed powder of P. nigrum L. and a teaspoon of processed sugar	leucorrhea, increasing sperm in semen and act as aphrodisiac.	
the first front of <i>Elephanopus scaber</i> L. long with 21 hage, mental complaints, menormagia, leucormenters, and only consumed with one glass of raw cow's milk on an empty stomach, twice every day for an empty stomach, twice every day for and only consumed with one glass of raw cow's milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach, twice every day for a milk on an empty stomach that in the stomach and the steed with one glass of raw cow's and district every day for an empty stomach and the find the intital volume to every day for a milk on an empty stomach and every stomach and one and the stomach and every and parties are made into a posts and administered only for an empty stomach and every and parties are made into a posts and administered only for a post and every and parties are made into a post and every and parties are made into a post and every and parties are made into a post and every and parties are made into a post and every and parties are made into a post and every and parties, foreign and parties are made into a post and every and parties, foreign and parties, foreign and parties, foreign and parties, foreign and parties are made into a post and every and parties, foreign and parties, foreign and parties are made into a post and every and parties, foreign and parties of characters of characters and parties, foreign and parties, foreign and parties, foreign and parties, foreign and parti					
fueled P. Signature L. seeds as ground and taken orally with 250mL of raw cow milk on an empty stormach with 250mL of raw cow milk on an empty stormach with cere of any decided in Figure L. Seed as a ground to powder and orally consumed with one glass of raw cowr's milk on an empty stormach, twice every day for 3 weeks.  20 of Perecorpus mansupium Roxb, fresh stem bank is milk on an empty stormach twice every day for 3 weeks.  20 of Perecorpus mansupium Roxb fresh stem bank is boiled in It of water until the volume reserves about one fifth of the initial volume. One one fifth of the initial volume. One one of this one fifth of the initial volume. One one of this one fifth of the initial volume. One one of this one fifth of the initial volume. One one of this one fifth of the initial volume. One one of the one of this are decortion and one of synghum are and administered orally for 7-3 days.  Roots of Tylephora asthmatica with P. nigrum I. somewhered forally for 7-3 days.  P. nigrum is given along with seven consumed in powdered P. nigrum and said.  P. nigrum is given along with seven orally, two to three tries along or the powder orally for 7-3 days.  P. nigrum is given along with common said.  P. nigrum is given along with p. nigrum L. Milmosa  Delifycowcler and Hibbicus rosa-sinensis. L. is prepared.  Oal/Powcel and th		Seed	10 g fresh root of <i>Elephantopus scaber</i> L. long with 21	Spermatorrhea, leucorrhea, ametror-	
Or or two Mangifer indica L kernels along with seven or 21 dried P nigrum L. seeds are ground to powder and only consumed with one glass of a-w. cows and only consumed with one glass of a-w. cows and to only consumed with one glass of a-w. cows and to only consumed with one glass of a-w. cows and to only consumed with one glass of a-w. cows and to only consumed with seven powdered dried seeds of Percorators marchigina. Rock fresh stem bank is been anopy stomach and in the cotton along with seven powdered dried seeds of Percorators marchiginal may be a consumed only on an empty stomach and in the cotton along with seven powdered dried seeds of Percorators marchiginal may be a consumed only on an empty stomach and in the cotton along with seven powdered dried seeds of Propogram commit lean, and gailify are made into a passe of Andhord worked New Statem of Sypagum commit lean, and gailify are made into a passe and deministration of Commun sortum L. with vater and configuration of Commun sortum L. with P. nigrum I. and decoration of Commun sortum L. with P. nigrum A mixture of Ciscampelos pareing, P. nigrum L are crushed and mixed with P. nigrum and palingur.  Inferior of Propogram considered P. nigrum A mixture of Ciscampelos pareing, P. nigrum L are crushed and mixed with P. nigrum and the product is onally taken.  Inferior of P. nigrum L are crushed and mixed with P. nigrum and the product is onally taken.  Inferior of P. nigrum L are crushed and mixed with P. nigrum and the product is onally taken.  Inferior of P. nigrum L are crushed and mixed with P. nigrum L and this cross sinemask L. is prepared. P. and the product is onally taken.  Inferior of P. nigrum L are crushed and mixed with P. nigrum L and deministration product is onally taken.  Inferior of P. nigrum L are crushed and mixed with P. nigrum L and this cross sinemask L. is prepared. P. and this cross sinemask L. is prepared. P. and this cross sinemask L. is prepared. P. and this cross and product is onally taken.  In the constant of Ciscampelos parei			dried <i>P. nigrum</i> L. seeds are ground and taken orally with 250 mL of raw cow milk on an empty stomach	rhagia, menstrual complaints, menor- rhagia and dysmenorrhea.	
One of two Manging in office. Lemens along with seven on the amount of powder and only consumed with one glass of raw cow/s male on an empty stomach, twice every day for a weeks.  20 of Percoarpus maraplium Robine teaches about milet on an empty stomach, twice every day for a weeks. 20 of Percoarpus maraplium Robine teaches about one tiff of the initiat loutine. One cup of this other initiat loutine. One cup of this one on empty stomach stored in potential or an empty stomach and stored or an empty stomach in the volume reaches about mercorthagia, amenorithea, leutor-bolled in 1.1 of water until the volume reaches about one cup of this one cup of			twice per day.	`	
and orally consumed with one gass of raw cowis  and orally consumed with one gass of raw cowis  and orally consumed with one gass of raw cowis  and orally consumed with one gass of raw cowis  and admitisted coally or a pair a standard and admitisted coally for 2-3 days.  Any and a minister and ordered to response to yet herbal medicine prepared by traditional healers using a definite or for minister and core or strength or a standard and admitister or coal mown with common salt.  An instrum of Cssampelos pareira, p. nigurm L. are crushed and mixed with  An inter of to sigurum L. are crushed and mixed with  An inter of to rigurum L. are crushed and mixed with  An inter of the intial volume. See and permitis and pale and the product is orally taken.  An inter of the intial volume, and the product is orally taken.  An inter of orall product is orally taken.  An inter orall product is orally taken.  An interior prepared by traditional healers using the and the product is orally taken.  An interior prepared by traditional healers using the and the product is orally taken.  An interior prepared by traditional healers using the and the product is orally taken.  An interior prepared by traditional healers using the and the product is orally taken.  An interior prepared by traditional healers using the product is orally taken.  An interior prepared by traditional healers using the and the product is orally taken.  An interior prepared by traditional healers using the product is orally taken.  An interior prepared by traditional healers using the product is orally taken.  An interior prepared by traditional healers using the product is orally taken.  An inter		Seed	One or two Mangifera indica L. kernels along with seven	Dysmenorrhoea, menorrhagia, leucor-	
milk on an empty stomach, twice every day for 3 weeks.  20 g of Prenocarpus marsupium Roxb, fresh stem bark is boiled in 1 Ld water until the volume reaches about one difful of the initial volume. One up of this police in 1 Ld water until the volume reaches about one fifth of the initial volume. One up of this and dark seen powdered acide, seeds of P. nigrum L. is consumed in propertion along with seven powdered or lay, two to three times daily for 3 weeks.  Leaf paste of Adharoda vasica Nees, is mixed with P. P. nigrum L. and garlic are made universed or ally for 2 a days.  Rost sof Vipoption activation and salt. An and administered or ally for 2 a days.  P. nigrum is given along with common salt. An and parties and coffee is prepared. Or somethe test and coffee is prepared. An ingram and salt. An and parties and palmour or Ciscampeles pareins. P. nigrum L. without and palmour of Ciscampeles pareins. P. nigrum L. and palmour of Ciscampeles pareins. P. nigrum L. and palmour of Ciscampeles pareins. P. nigrum L. are crushed and mixed with the product is orally taken.  In first the product is orally taken. In digestion, loss of appetite, waist  In first to the indigestion, loss of appetite, waist  In first to the indigestion, loss of appetite, waist  In first the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion, loss of appetite, waist  In first to the product is orally taken. In digestion is prep			or 21 dried <i>P. nigrum</i> L. seeds are ground to powder and orally consumed with one glass of raw cow's	rhea, metrorrhagia, menstrual com- plaints and spermatorrhea	
20 g of Preocarpus marsupium Roxb, fresh stem bark is beneatornhea, bucorbolled in 1 of water until the volume reaches about one fifth of the initial volume. One up of this passe of the dialy for 3 weeks.  Leaf passe of Adharoda vasica Nees, is mixed with P. P. Injurum L. is onsumed only two to three times daily, for 3 weeks.  Leaf passe of Adharoda vasica Nees, is mixed with P. P. Injurum L. is onsumed only two to three times daily for 3 weeks.  Ross of Vipophora osthanatica with P. Injurum L., fruits of Syzgium cumin Lam. and garlic are make along a paste and administered only for 2 -3 days.  P. Injurum Li and administered only for 2 -3 days.  P. Injurum, dried ginger and palm sugar are mixed along with vacered P. Injurum and salt.  P. Injurum is given along with common salt.  P. Injurum is given along with given and the product is orally taken.  Injurum is given and the product is orally taken.  Injurum decentage and the product is orally taken.  Injury decentage and the product is orally take			milk on an empty stomach, twice every day for 3 weeks		
boiled in 1. of water until the volume reaches and empty stome diffused in the initial volume. One cup of this and impotency of the initial volume. One cup of this and impotency of the initial volume. One cup of this and impotency of the initial volume. One cup of this and impotency of the initial volume. One cup of this additional breakers powdered by traditional breakers and paints and pailified and paste of Adhatodo vosican Ness. is mixed with P. inigrum. L. fruits of Syzglum cumini Lam, and gallified employed and paste and administered orally for 2–3 days.  P. inigrum, cumini Lam, and gallified employed and principle prepared.  P. inigrum, cumini Lam, and gallified employed and principle prepared orally for 2–3 days.  P. inigrum, cumini Lam, and gallified employed and principle prepared orally for 2–3 days.  P. inigrum, cumini Lam, and gallified employed and principle prepared orally for 2–3 days.  P. inigrum, cumini Lam, and gallified employed and principle prepared orally common salt.  Omelete is made using powdered P. inigrum and salt.  P. inigrum, dired ginger and palm sugar are mixed along with common salt.  Omelete is made using powdered P. inigrum and salt.  P. inigrum, dired ginger and palm sugar are mixed along with common salt.  Omelete is made using powdered P. inigrum and salt.  P. inigrum, dired ginger and palm sugar are mixed along with common salt.  Omelete is made using powdered P. inigrum and salt.  P. inigrum, dired ginger and palm sugar are mixed along with common salt.  Omelete is made using powdered P. inigrum m. I are crushed and mixed with the pudder it and the product is orally taken.  In indigestion, loss of appetite, waist the product is orally taken.  In indigestion, loss of appetite, waist the product is orally taken.  In indigestion, loss of appetite b. inigrum and the product is orally taken.  In indigestion and product is orally taken.  In indigestion and product is orally taken.  In indigestion and the product is orally taken.  In indigestion and in intermination and financia		7000	30 of Diancarnic marcinging Dook fresh stom book is	Characteristic constant control	
one fifth of the initial volume. One cup of this decordor along with seven powdered dried seeds of the decordor along with seven powdered dried seeds of the initial volume. One cup of this and decordor and with seven powdered dried seeds of the decordor of along with seven powdered dried seeds of the decordor of a page and a definitial volume. It is consumed or and palm super and coding in a page and a definitial work of the decordor of spragium cuminic lam, and galic are made into a past and administrated valify for 2-3 days.  Roots of Spragium cuminic lam, and galic are made into a past and administrated valify for 2-3 days.  Pugurant, dried ginger and palm supar are mixed along with water and coffee is prepared. Omelete is made using powdered P. nigrum and salt.  Pugurant, dried ginger and palm supar are mixed along with water and coffee is prepared. Omelete is made using powdered P. nigrum and salt.  Pugurant, dried ginger and palm supar are mixed along with water and coffee is prepared. Omelete is made using powdered P. nigrum and salt.  Pugurant and coffee is prepared by traditional healers using P. nigrum is give along with common salt.  Pugurant and palmogur.  Leaf decoction of Coffee is prepared. A mixture of Cissampelos pareira. P. nigrum L. Milmosa and palmogur.  A mixture of Cissampelos pareira. P. nigrum L. Milmosa and palmogur.  A mixture of Cissampelos pareira. P. nigrum L. Milmosa and palmogur.  Pugurant and Hibiscus rosa-sinerisis. L. is prepared.  Oral/Powder.  Oral/Powder.  Indigestion, loss of appetite, waist Rout and Panda 2010 pain, cough and cold, diarrhea.		ספפר	20 g of <i>recocal pas marsuphum</i> Noxo. nest stell bark is boiled in 1L of water until the volume reaches about	spermatuna, spermatormea, reucor- rhea, metrorrhagia, amenorrhea, dvs-	
decoction along with seven powdered dried seeds of and impotency  P. Injurum. L. is consumed orally on an empty stomach daily for 3 weeks.  Leaf paste of Adhatodra vasical Neess, is mixed with P. Injurum and salt.  Program L. made into pills taken orally, two to three rimes daily.  Roots of Pupports activated vasical Neess is mixed with P. Injurum and salt.  P. Injurum (Pupports and paint sugar are mixed along with water and coffier is prapared.  P. Injurum (Pupports and paint sugar are mixed along with water and coffier is prapared.  P. Injurum (Pupports and paint sugar are mixed along with water and coffier is prapared.  P. Injurum (Pupports and paint sugar are mixed along with common salt.  P. Injurum is given along with common salt.  P. Injurum (Pupports is prepared.)  I. Injurum (Pupports is prepared.)  I. I			one fifth of the initital volume. One cup of this	menorrhea, menorrhagia	
Left paste of Adharoda vaceks.  Left paste of Adharoda vaca Nees, is mixed with P. Ingram of Adharoda vaca need into pills taken orally, two to three times daily.  Roos of Typophoroa extinantica with P. nigrum L., fruits of P. Sygium cumin Lam. and garlie are made into a paste and administered orally for 2–3 days.  P. nigrum, ded digines and paint sugar are mixed along with common salt.  P. nigrum and soffere is prepared. Omelette is made using powdered P. nigrum and salt. P. nigrum is given along with common salt.  NI  NI  NI  Leaf decoction of Ocimum sanctum L.with P. nigrum Leaf decoction of Ocimum sanctum L.with P. nigrum and palmagur A mixture of Cissampelos pareira. P. nigrum L. with P. nigrum and palmagur A mixture of Cissampelos pareira. P. nigrum L. with P. nigrum and palmagur A mixture of Cissampelos pareira. P. nigrum L. with P. nigrum and dematopathy pudica L. and Hibiscus rosa-sinensis L. is prepared. Oral/Powder  The fruits of P. nigrum L. are crushed and mixed with ghee and the product is orally taken. NI  NI  NI  Rout and Palma 2010 Seraver Stomach ache, indigestion Stomach ache indigestion Stomach ache indigestion Stomach ache indigestion Stomach ache S			decoction along with seven powdered dried seeds of <i>P. nigrum</i> L. is consumed orally on an empty stom-	and impotency	
Leaf paste of Adhatoda vasica Nees, is mixed with P. Items based of Adhatoda vasica Nees, is mixed with P. Items daily.  Roots of Tylophora asthmatica with P. nigrum L., fruits of P. nigrum and administered orally for 2-3 days.  P. nigrum, dired ginger and palms ugar are mixed along with water and coffee is prepared.  Omelette is made using powdered P. nigrum and salt.  P. nigrum, dired ginger and palms ugar are mixed along with water and coffee is prepared.  Omelette is made using powdered P. nigrum and salt.  P. nigrum is given along with common salt.  P. nigrum is given and mixed with P. nigrum  A mixture of Cissampelos pareira. P. nigrum  A mixture of Cissampelos pareira.  P. nigrum is given and the product is orally taken.  Indigestion, loss of appetite, waist are crushed and mixed with pagin, cough and cold, diarrhea  P. Sivasankari, Arandhuia 2010  Semual et al. 2016  Guid and Femil			ach daily for 3 weeks.		
times daily.  Roots of Tylophora astimatica with P. nigrum L. fruits of Sygyalum cuminic Lam. and garlic are made into a paste and administered orally for 2–3 days.  P. nigrum, dried ginger and palm sugar are mixed along with common salt.  P. nigrum, dried ginger and palm sugar are mixed along with common salt.  P. nigrum, dried ginger and palm sugar are mixed along with common salt.  P. nigrum, dried ginger and palm sugar are mixed along with common salt.  P. nigrum is given along with and palmar 2014  P. nigrum is given along with p. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar.  A mixture of Cissampelos pareira, P. nigrum  and palmar 2014  P. propareira, P. nigrum L. Mimosa  Pever and palmar 2014  Propareira and remita and mixed with  Sinasankari, Anandharaj, ar  Gunasekaran 2014  Salakia et al. 2006  Gunasekaran 2010  Gunasekaran 2010  Gunasekaran 2010  Sinasankari, Anandharaj, ar  Gunasekaran 2010  Gunasekaran 2010  Gunasekaran 2		Z	Leaf paste of Adhatoda vasica Nees, is mixed with P.	Fever	Mahishi, Srinivasa, and Shivana 2005
Roots of Tylophora asthmatica with P. nigrum L., fruits of Stayglum cumini Lam. and garlic are made into a paste and administered orally for 2–3 days.  Paste and administered orally for 2–3 days.  Personand administered orally for 2–3 days.  Cold and coughs and coughs are mixed along with water and coffee is prepared.  Personand and consumed in powder and program safe.  Personand and experiency izanoides, honey and P. nigrum and palmgur.  A mixture of Cissampelos pareira, P. nigrum L., Mimosa pulk prodred L. and Hibiscus rosa-sinensis L. is prepared.  Oral/Powder  Oral/Powder  A mixture of Cissampelos pareira, P. nigrum L. are crushed and mixed with ghee and the product is orally taken.  Indigestion, loss of appetite, waist and Panda 2010  Indigestion, loss of appetite, waist and Panda 2010  Pastal and deministered orally for L. and Panda 2010  Indigestion, loss of appetite, waist and Panda 2010  Indigestion and palmgur.  Indigestion of Cisampelos pareira P. pigrum L. are crushed and mixed with ghee and the product is orally taken.  Indigestion, loss of appetite, waist and Panda 2010  Pastal and Figura P. and Panda 2010  Pastal and Panda 2010  Pastal and Femilia 2012  Sermand Femilia 2012  Jeeva and Femilia 2012  Jeeva			times daily.		
of <i>Syzgum</i> cumin Lam. and garifc are made into a paste and administered orally for 2–3 days.  P. nigrum, ited ginger and palm sugar are mixed along with water and coffee is prepared.  Omelette is made using powdered P. nigrum and salt.  P. nigrum, ited ginger and palm sugar are mixed along with water and coffee is prepared.  Onally consumed in powder Herbal medicine prepared by traditional healers using Periveria zizanoides, honey and P. nigrum Leaf decoction of Ocimum sanctum L.with P. nigrum A mixture of Cissampelos pareira, P. nigrum L. A mixture of Cissampelos pareira, P. nigrum L. are crushed and mixed with papatits, flatulence, indigestion The fruits of P. nigrum L. are crushed and mixed with ghee and the product is orally taken.  Ni medicine prepared by traditional healers using Stomach ache indigestion Vijayakumar 2014 Semwal et al. 2014 Scabies Scabies Stabies Stabies Amandharaj, and Gunasekaran 2014 Stabies Amandharaj, and Gunasekaran 2014 Stabies Stabies Stabies Amandharaj, and Stabies Stabies Amandharaj, and Stabies Stabies Amandharaj, and Gunasekaran 2014 Stabies Amandharaj and Chaudhuri Cough and could, diarrhea		Z	Roots of Tylophora asthmatica with P. nigrum L., fruits	Jaundice	
P. nigrum, dried ginger and palm sugar are mixed along with water and coffee is prepared.       Cold and coughs onelette is made using powdered P. nigrum and salt.       Cold and coughs are mixed sordered P. nigrum and salt.       Cold and coughs are given along with common salt.       Stomach active (Toothacke)       Yabesh, Prabhu, and Yabesh, Prabhu, and Stomach disorders         N In Charly consumed in powder Herbal medicine prepared by traditional healers using Vetiveria zizanoides, honey and P. nigrum Leaf decoction of Ocimum sanctum L. with P. nigrum and palmgur and palmgur A mixture of Cissampelos pareira, P. nigrum L. Mimosa pudica L. and Hibiscus rosa-sinensis L. is prepared.       Niral hepatitis, flatulence, indigestion palm, cough and cold, diarrhea       Singh and Femila 2014         A mixture of Cissampelos pareira, P. nigrum L. Mimosa pudica L. and Hibiscus rosa-sinensis L. is prepared.       Viral hepatitis, flatulence, indigestion and dermatopathy       Sivasankari, Anandharaj, are dematopathy         The fruits of P. nigrum L. are crushed and mixed with ghee and the product is orally taken.       Indigestion, loss of appetite, waist       Rout and Panda 2010         NI       NI       Palma Panda 2010       Palma Panda 2010			ot <i>syzygium cumini</i> Lam. and gariic are made into a paste and administered orally for 2–3 days.		
with water and coffee is prepared.  Omelette is made using powdered <i>P. nigrum</i> and salt.  Puly consumed in powder along with common salt.  National probable is given along with common salt.  National probable is given along with common salt.  National probable is given along with common salt.  Stomach disorders  Singh and Chaudhuri 2018  Semwal et al. 2014  Semwal et al. 2014  Semwal et al. 2014  Stomach ache, indigestion  Singh and Chaudhuri 2018  Semwal et al. 2014  Stomach ache, indigestion  Singh and Chaudhuri 2018  Semwal et al. 2014  Stomach ache, indigestion  Singh and Chaudhuri 2018  Semwal et al. 2014  Stomach ache, indigestion  Singh and Chaudhuri 2018  Semwal et al. 2014  Stomach ache, indigestion  Singh and Chaudhuri 2018  Semwal et al. 2014  Stomach ache, indigestion  Singh and Chaudhuri 2018  Semwal et al. 2014  Stomach ache, indigestion  Singh and Chaudhuri 2018  Semwal et al. 2014  Semwal		N		Cold	Jeeva and Femila 2012
Omelette is made using powdered <i>P. nigrum</i> and salt.  Penigrum is given along with common salt.  Stomach disorders  Orally consumed in powder Herbal medicine prepared by traditional healers using  Vetiveria zizanoides, honey and P. nigrum Leaf decoction of Ocimum sanctum L.with P. nigrum and palmigur A mixture of Cissampelos pareira, P. nigrum L., Mimosa  Pudica L. and Hibiscus rosa-sinensis L. is prepared. Oral/Powder  The fruits of P. nigrum L. are crushed and mixed with The fruits of P. nigrum L. are crushed and mixed with  Indigestion, loss of appetite, waist  NI  Rout and Panda 2010 pain, cough and cold, diarrhea		:	with water and coffee is prepared.	-	
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Leg decoction of Ocimum sanctum L.with P. nigrum  and palmgur  A mixture of Cissampelos pareira, P. nigrum L., Mimosa  pudica L. and Hibiscus rosa-sinensis L. is prepared.  Oral/Powder  The fruits of P. nigrum L. are crushed and mixed with  ghee and the product is orally taken.  Indigestion, loss of appetite, waist  Scapies  Indigestion, loss of appetite, waist  Fever  Seminary and Chaudhuri 2018  Semwal et al. 2014  Gunasekaran 2014  Scabies  Salkia et al. 2006  glunasekaran 2014  Salkia et al. 2006  glunasekaran 2017  Pain, cough and cold, diarrhea		Z	Herbal medicine prepared by traditional healers using	Stomach ache	Vijayakumar 2014
and palmgur A mixture of Cissampelos pareira, P. nigrum L., Mimosa  A mixture of Cissampelos pareira, P. nigrum L. is prepared.  Oral/Powder  Oral/Powder  The fruits of P. nigrum L. are crushed and mixed with ghee and the product is orally taken.  Indigestion, loss of appetite, waist  A mixture control  Sivasankari, Anandharaj, ar  Gunasekaran 2014  Scabies  Scabies  Saikia et al. 2006  Judigestion, loss of appetite, waist  Rout and Panda 2010		Z	Leaf decoction of <i>Ocimum sanctum</i> L.with <i>P. nigrum</i>	Fever	Singh and Chaudhuri 2018
A mixture of <i>Cissampelos pareira</i> , <i>P. nigrum</i> L., <i>Mimosa</i> Birth control  pudica L. and <i>Hibiscus rosa-sinensis</i> L. is prepared.  Oral/Powder  Oral/Powder  The fruits of <i>P. nigrum</i> L. are crushed and mixed with  ghee and the product is orally taken.  Indigestion, loss of appetite, waist  NI  Rout and Panda 2010  pain, cough and cold, diarrhea			and palmgur		,
Oral/Powder  Viral hepatitis, flatulence, indigestion Sivasankari, Anandharaj, ar  and dermatopathy Gunasekaran 2014 Scabies Scabies ghee and the product is orally taken.  Indigestion, loss of appetite, waist NI Rout and Panda 2010 pain, cough and cold, diarrhea		Z	A mixture of Cissampelos pareira, P. nigrum L., Mimosa pudica L. and Hibiscus rosa-sinensis L. is prepared.	Birth control	Semwal et al. 2014
The fruits of <i>P. nigrum</i> L. are crushed and mixed with Scabies Sabies Sabies Salkia et al. 2006  Salkia et al. 2006  Indigestion, loss of appetite, waist Rout and Panda 2010  pain, cough and cold, diarrhea		Fruit	Oral/Powder	Viral hepatitis, flatulence, indigestion	Sivasankari, Anandharaj, and Gimasekaran 2014
Indigestion, loss of appetite, waist Rout and Panda 2010 pain, cough and cold, diarrhea		Fruit	The fruits of <i>P. nigrum</i> L. are crushed and mixed with	Scabies	Saikia et al. 2006
		Seed, Fruit		Indigestion, loss of appetite, waist	Rout and Panda 2010
				pain, cough and cold, diarrhea	

Country	Part of plant used	Mode of preparation/ dosage	Ailments/Medicinal use	References
	Z	Fruit powder of <i>Helicteres isora</i> L. is boiled with <i>P. nig-</i> rum, allium sativum rhizome and gingelly oil	Earache	Kumar, Ayyanar, and Ignacimuthu2007
	Seed	ns applied. Powdered seeds are orally administered.	Cough, bronchial disorders and as antidote against snake bite	
	N	Root paste of Plesmonium margaritiferum is mixed with	Dysentery	Sen and Behera2008
	Z	P. nigrum is taken two times per day. Bark decoction of Pterospermum xylocurpum is mixed with P. nigrum powder and is taken two times	Infantile diarrhea	
	Fruit	per udy. Decoction of leaves of <i>Trichosanthes dioica</i> Roxb. and <i>P</i> .	Diarrhoea	
	Z	nigrum fruit powder is taken 3–4 times daily.	<u> </u>	Paisking and Chivana 2010
	Ξ	Stein prece of Coasia duricular Emil. is ground with leaves of Leucas aspera Spreng., P. nigrum Linn. and Allium sativum Linn. into paste is taken orally for 3—4 davs		najaruillai ailu Jiivailliazoto
	Seed	The dried seeds of <i>P. nigrum</i> are taken orally.	Throat infection	Ignacimuthu, Ayyanar and
	N	Seed powder of <i>Annona reticulata</i> L. is mixed with 3 g of <i>P. niarum</i> .	Spoiling of pregnancy up to 3-4 months duration	Abe and Ohtani2013
	Z	3g of leaf paste of Capparis zeylanica L. is mixed with 2g of P. nigrum paste and applied for slight boiling before hed.	Breast swelling	
	Seed	3 mL of the fresh juice of stem bark of <i>Crateva nurvala</i> is mixed the fresh juice of stem bark of the second is taken by women and is	Contraceptive (1 <sup>st</sup> seven days of menstrual cycle)	
	Z	5g of the stem juice of Saccharum officinarum L. with	Constitutional disorder	
	Z	1 g or <i>F. migram</i> paste. 3 mL of the decocted <i>Sida acuta</i> leaf is mixed with 2 g	Swelling of scrotum	
	:	r. nigrum paste and I mL of lime water and is taken two times per day after food for a week.	; ; ;	
	Z	About 15 mL of <i>Vitex negundo</i> L. decocted root bark together with a paste of 21 <i>P. nigrum</i> is taken twice a dav after food for seven davs.	lyphoid Tever	
Bangladesh	Fruit	375 g of leaves and 375 g of stems of <i>Solanum barbisetum</i> are mixed with 12 g <i>P. nigrum</i> L. fruits, 12 <i>Cinnamonum tamala</i> leaves, 2 <i>P. longum</i> L. fruits,	Influenza	Rahmatullah et al. 2012
		rock salt, powdered dried bark of <i>Cinnamomum</i> verum and 25 g of crystalline sugar is placed in boiling water in an earthen pot. After the decoction has been cooled and the water is filtered through a piece of cloth and the filtrate is orally administered		
	Seed	to patients.  Powdered bark of <i>Diospyros peregrina</i> L is ground with 2-5 seeds of <i>P. nigrum</i> L. and applied to gout	Chest pain due to gout	Rahmatullah et al. 2013
	Seed	anected areas. Leaves of <i>Eleusine indica</i> (L.) are macerated with seeds of <i>P. nigrum</i> L. and applied to painful areas once	Pain in spinal cord	
	Seed	Macerated whole plants of <i>Sida cordata</i> are mixed with powdered seeds of <i>P. nigrum</i> L. and applied around the cides of the abscace	Abcess	
	Seed	tile sides of tile abscess.		

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and the just contained in mined with 10-15 pow- died eeds of b, nigural. L and administered only 3 stures all bit of columbs to make with 10-15 pow- fered eeds of b, nigural. L and administered only 3 stures all by one worthout L and administered only 8 a half route of soluministered strategies of by nigural. L and routed with two and a half routed and produced for the start day for 3 weeks.  The pilks series a prophylata for the start day for 3 weeks.  The pilks series a prophylata for the start day for 3 weeks.  The pilks series a prophylata for the start day for 3 weeks.  The pilks series a prophylata for the start day for 3 weeks.  The pilks series a prophylata for the start day for 3 weeks.  The pilks series a prophylata for the start day for 3 weeks.  Proposed for the color of color of color of the pilks of the start day for 3 weeks.  Rous of addient indicator of of (prosonis perior)  Rous of addient indicator may of the pilks of the start day of the star			The roots of Leucas aspera (Willd.) Link are macerated	Severe headache due to fever,	
deed each of P. pury Stormer,  Powerer each of P. pury Stormer,  Read of Read of Program Learner and Programmer and Programmer Stormer			and the juice obtained is mixed with 10–15 pow-	dog bite.	
forested seeds of P. gragam L are taken with two and a half of sease of P. gragam L are taken with two and a half once of Sodium valuation.  For seed of Rouwolfo seperation L are carbon with two and a half once of Rouwolfo separation L are carbon with seeds.  For seed of Rouwolfo separation L are carbon with seeds.  Fig. 15 and 1			dered seeds of P. nigrum L. and administered orally 3		
Provieted sets of 6 of fuginar, Le tra class with two and a half rost of Salaman wigningtown. Le tra classed with seeds of 6 salaman wigningtown. Le and informers. Zaglete discinded and macerated from yet and early to the mixture to form pairs. Three piles are to be taken day for 3 weeks.  The piles see to per pairs from mixture to form pairs. The piles seed mixture to form macerated from the form of the mixture to form the piles are to be taken day for 3 weeks.  The piles see to per pairs from mixture to form the piles from			times daily on an empty stomach		
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The pill serve of the cited reflective in the cited of th			macerated. Honey is added to the mixture to form		
Figure 1 per line service as prophylates from itside  Fulls service as prophylates from itside  Fulls service as prophylates from itside  Fulls of both Colocation mynobredials when the first of the single f			pills. Three pills are to be taken daily for 3 weeks.		
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Or fun to the transfer of the Advances agent of the Advance of the Advanced funct of the Advanced function for an empty storage of the activities of the act			and 1 and concepts and taken things for 7 days		
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neacerated cot of Advancants capear. The mixture is taken on an empty somach for one day.  Robos of Abusino nankurun soots of disconsis perture.  Robos of Resultan in and or which 42 pills  are obtained to me parter with a cold of which 42 pills  are obtained to me parter with a cold of which 42 pills  are obtained to me parter with a cold of which 42 pills  are obtained to me parter with a cold of which 42 pills  are obtained to me parter with a cold of the cape of Motors  and chained is a pill seem that mediately.  20 finate of P. nightum, one handled of leaves of Motors  and cold of P. Sevel Africatived area as a thick paster and cold-and and measured. The mixture is applied  and bandaged for a week.  Robos of Pergulation demain are meacrated with 2.3-3  seeds of P. nightum routs from the mixture is applied  and bandaged for a week.  Robos of Pergulation demain are meacrated with 2.3-3  seeds of P. nightum routs from the mixture with a cold of the cold		Fruit	One powdered fruit of $P$ , nigrum is mixed with one	Menstrual pain	Biswas et al. 2011
Helden on empty stomated for one day.  Roots of <i>Abusilon indicum</i> ; roots of <i>Glycocamis gente</i> .  Phyliq roots of <i>Elevater indica</i> , and roots of the mean and macated.  Amounthus spinous are mixed and macated.  Another in mean and mixed and macated.  Sugar and 21 powdered fruits of <i>P. nigum</i> are then added to the mean and mix and of with Cup of a water three times per day of 2 veeds.  Several Arcialcohan mixed leavy.  Several Arcialcohan mixed leavy are mixed and macated with Cup of or largemy and the juice obtained is only taken immediately.  20 fruits of P. nigum, one hardful of leaves of Moust in the macated and 23-30 fruits of P. nigum, one hardful of leaves of Moust in the macated with 2-3 red of P. nigum fruits and east of Reveal Architectured area as a thick paste and conered with 1-0 pout of the page of the nigum fruit and 130 fortum metel L. Pills are made from the macate and mixed and macated and mixed in the macated and mixed in the mixed in the mixed of P. Septembra of Polygourun hydropper leaves are macated and mixed in the mixed of P. Septembra of Polygourun hydropper are macated and mixed in the mixed of P. Septembra of Polygourun hydropper are mixed fruit and fruits and fruit and fruit and fruit and fruit and fruit and fruit of P. nigum fruit. From the mixture, and the mixed of P. Septembra of Polygourun hydropper are mixed this are prepared from the mixture, and the macated land and the macated land the produced fruit of P. nigum fruit of P. nigum fruit of P. nigum fruit of P. nigum and the macated hills are prepared from the mixture, and the mixture and the macated hills are prepared from the mixture, and the mixture of Polygourun hydropper are mixed Hills are prepared from the mixture, and the mixture of Polygourun hydropper are mixed Hills are prepared from the mixture, and the mixture of P			macerated root of Achyranthes aspera. The mixture is		
Roas of Aburdion indicum, roots of Gyrcomis pentro- phyllo, note of Eleziane indicut, and macetaed. Amaranthas spinous are mixed and macetaed. Amaranthas spinous are mixed and macetaed. Augurand 12 prowdered fruits of P. inguin are then added to the macetaed mix and oi which 42 pills are obtained to pre lated with 42 pills.  Several Artsoloding indica leaves are mixed and macetaed to the macetaed mix and oi which 42 pills.  Several Artsoloding indica leaves are mixed and macetaed and the pilice of chosts. A fest mixture is applied to a week. The stream mixture is applied to a week of the pilice of the pilice of the pilice of the pilice of pili			taken on an empty stomach for one day		
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are obtained. One pill is to be taken with 1 cup of water three times per day for 2 weeks.  Several Advisorloriu mick nelaves are mixed and macer- ared with 2-3 futus of ingram and the buse obtained is only these immediately.  20 futuis of P. rigum, nor handful of leaves of Mouse indica, 50g rhizomes of Zingiber officinale and 25-30 dopps of oil prepared from seeds of Rossica compess in see mixed and maceraled. The mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture is applied and bandaged for a week. A fresh mixture. A foot mix are lake thritice daily. Foot 2-3 days. B foot 0.9 future of the control of the mixture. I pull is taken three times per perpared from the mixture. I pull is taken three times daily for 2-3 days.  Catarrh with cough  Catarrh with cough  Catarrh with cough			Sugar and 21 powdered fruits of <i>P. nigrum</i> are then		
are obtained. One pill is to be taken with 1 cup of water three times per day for 2 veeks. Several Aristolochia indica leaves are mixed and macer- ared with 2-3 futus of p. niguma mad the pixee obtained is onelly daken immediately. To fituits of p. niguma no handful of beaves of Mons. To fituits of p. niguma, no handful of beaves of Mons. To fituits of prepared from seeds of Brassica campestrifica, 30g rhizomes of Zingber arisitate is then applied to fractured area as a thick paste and compared from seeds of Brassica campestrificate of a veek. The providence of Zingber officinale and 35-30 drops of oil prepared from seeds of Brassica campestrificate of the Arish mixture is applied and bandaged for a veek.  Roots of Pequalization dender are macerated with 2-3 aceds of p. nigum, p. 181 are made from the macer- ated mix are taken thrice daily administered mimediately. Polygoum mydropiper leaves are macerated and mixed with 1 powdered P. nigum fruit. From the mixture, pills are prepared. One pill is taken three times per deformate macerated. Pills are prepared from the mixture. It is taken three times daily for 2 veeks.  I powdered fruit of P. nigum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2 veeks.  I powdered fruit of P. nigum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2-3 days.  Catarrh with cough			added to the macerated mix and of which 42 pills		
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Several Aristolochia inflore leaves are mixed and macerated which services are mixed and macerated by the continued area by a read with 2-3 fruits of P. niguran one handful of leaves of Mous inflored is onally taken immediately.  20 fruits of P. niguran, one handful of leaves of Mous inflored and Macental and December of Bossica campears of 10 prepared from seeds of Bossica campears of 10 prepared from seeds of P. nigural pain and bandaged for a week and macental mixed with 2-3 seeds of P. nigural pain fruits and 3 Detural metel L. root are each of P. nigural pain in thrice dally for 2-3 days.  2.5 g. P. nigural pain fruits from the mixed with 1 powdered P. nigural fruit of Polygonum hydropiper leaves are macented. Pills are prepared from the mixture. I pill is taken with 1 cup of waret thrice dally for 2 weeks.  1 powdered fruit of P. nigural mixture. I pill is taken with 1 cup of waret thrice dally for 2 weeks.  1 powdered fruit of P. nigural mixture. I pill is taken with 1 cup of waret thrice dally for 2 weeks.  1 powdered fruit of P. nigural mixture. I pill is taken with 1 cup of waret thrice dally for 2 weeks.  1 powdered fruit of P. nigural mixture. I pill is taken with 1 cup of waret thrice dally for 2 weeks.  1 powdered fruit of P. nigural mixture. I pill is taken with 1 cup of waret thrice dally for 2 weeks.  1 powdered fruit of P. nigural mixture. I is taken three times dally for 2-3 days.  Catarrh with cough			water three times her day for 2 weeks		
acted with 2-3 finds of P. nigura and the juice obtained is only taken immediately.  20 fuits of P. nigura, one handful of eaves of Mons.  10 fuits of P. nigura, one handful of eaves of Mons.  11 ind of Myristac form the macerated and based from the macerated and macerated and macerated and macerated with 2-3  12 seed of P. nigura L. Pils as made from the macerated and based of P. nigura L. Distance of P. nigura macerated plants are prepared. One of P. nigura and macerated plants of P. nigura and plants of P. nigura plants of P. nigura plants of P. nig			Course Arietalockia indica locuse and massa	\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	
a dece with 2.3 truits of P. ingrum and the juice obtained is only taken immediately.  2 of fuits of P. nigrum one handful of leaves of Monss in the consistency of oil prepared from seeds of Brossica camperation of seeds of Brossica camperation is then applied to fractured area as a thick paste and coveraged with 2.3 seeds of P. nigrum. It is lase made from the macerated with 2.3 seeds of P. nigrum. It is lasen three times per day for 2.3 day.  2.5 g. nigrum fruits and 3g Datura metel L. root are good out. It is called the mixture, pills are prepared. One pill is taken three times per day for 2.3 days.  2.5 g. nigrum in to Myristica finguras, 1 fruit of Propygonum hydropiper leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture, 1 pill is alsen with 1 cup of vater time daily for 2 weeks. It is taken three times defined from the mixture. It is taken three times daily for 2.3 days.  1. powdered fruit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2.3 days.		Frait	Several Aristolochia mara leaves are mixed and macer-	Shake Dite	
obtained is only taken immediately, a obtained is only taken immediately and 25–30 drous of oil prepared from seeds of <i>Broasia campest-fromes</i> of <i>Zingiber officinale</i> and 25–30 drous of oil prepared from seeds of <i>Broasia campest-fromes</i> are mixed and macerated. The mixture is applied and bandaged for a week.  Rous of <i>Pergutaria deamia</i> are macerated with 2–3 seeds of <i>P. nigrum</i> . List and 3 gourd metal. Tool are ground, it is orally administered immediately.  Polygonum hydropiper leaves are macerated and mixed with 1 powdered <i>P. nigrum</i> fruit is only seeds. On pill is taken three times per day for 2–3 days.  2 go for <i>P. nigrum</i> . In anottal leaves of <i>Polygonum hydro</i> .  Polygonum hydropiper are mixed. Pills are prepared from the mixture, and the macerated leaves of <i>Chologon decision</i> are mixed. Pills are prepared from the mixture, it is taken three times daily for 2–3 days.  1 powdered fruit of <i>P. nigrum</i> and the macerated leaves of <i>Chologon decision</i> are mixed. Pills are prepared from the mixture, it is taken three times daily for 2–3 days.  1 powdered fruit of <i>P. nigrum</i> and the macerated leaves of <i>Chologon decision</i> are mixed. Pills are prepared from the mixture, it is taken three times daily for 2–3 days.			ated with 2–3 fruits of $P$ . nigrum and the juice		
10 fuits of P. nigum. one handful of leaves of Mouss index 2.30 dops of oil prepared from seeds of Boasica campest- nia mixed and macented. The mixture is then applied to facture area as a thick paste and covered with a piece of cloth. A fresh mixture is applied and bandaged for a week.  Roots of Pergularia deemia em necerated with 2.3 seeds of P. nigum L. Pills are made from the macer ared mixed by the pound it is orally administered immediately.  Polygound it is orally administered from the mixture. I pill is taken with 1 cup of varieth from the mixture. I pill is taken with 1 cup of of varieth from the mixture. It is taken three times daily for 2 webs.  I powdered fruit of P. nigum and the macentated leaves of Chrodon dorylon are macentaet. Pills are prepared from the mixture. It is taken three times daily for 2 -3 days.  Catarth with cough			obtained is orally taken immediately.		
drops of oil prepared from seeds of Brasisca campestris are mixed and macerated. The mixture is then applied to fractured area as a thick paste and covered many populated from seeds of Corb. A fresh mixture is applied and bandaged for a week.  Roots of Pergularia daemia are macerated with 2–3 seeds of Pr. ingrum. Pulls are part mixed and mixed amy for 2–3 days.  2.5 p. nigrum fuits and 3 g Datura metel L. root are ground. It is ofally administered immediately. Polygonum hydropiper leaves are macerated and mixed with 1 powdered P. nigrum fuit. From the mixture, pills are paper. Of P. nigrum, 1 handful leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. I pill is taken with 1 cup of water thrice daily for 2 weeks.  1 powdered froit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. I pill si taken three times daily for 2–3 days.  1 powdered froit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. I is taken three times daily for 2–3 days.  1 powdered froit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. I is taken three times daily for 2–3 days.		Fruit	20 fruits of <i>P. nigrum</i> , one handful of leaves of <i>Morus</i>	Bone fracture	
drops of oil prepared from seeds of <i>Brassica campest-fis</i> are mixture is then applied to fractured area as a thick paste and covered with a piece of cloth. A fresh mixture is applied and bandgaed for a week.  Roots of <i>Pergularia demini are</i> macerated with 2-3 seeds of <i>P. nigrum</i> furits and 39 <i>Garuma metel</i> L. root are ground. It is orally administered immediately.  Polygorum hydropiper leaves are macerated and mixed with 1 powdered <i>P. nigrum</i> fult. From the mixture, pills are prepared. One pill is taken three times per day for 2-3 days.  2 g of <i>P. nigrum</i> , 1 handful leaves of <i>Polygonum hydro-piper leaves</i> of <i>Cynodon dactylon</i> are macerated. Pills are prepared from the mixture. It is taken three times daily of value are mixed. Pills are prepared from the mixture. It is taken three times daily for 2-3 days.  Catarrh with cough			indica, 50 a rhizomes of Zingiber officinale and 25–30		
ris are mixed and macerated. The mixture is then applied to fractured are as a thick paste and covered with a piece of cloth. A fresh mixture is applied and bandaged for a week.  Roots of Pergularia dremia are macerated with 2-3 seeds of P. niguran L. Pills are made from the macerated and mixed with 1 powdered P. niguran fruits and 3g Datura metel L. root are ground. It is orally administrated immediately.  2.5 g P. niguran fruits and 3g Datura metel L. root are ground. It is orally administrated immediately. Polygonum hydropiper leaves are macerated and mixed with 1 powdered P. niguran fruit from the mixture, pills are perpared. One pill is taken three times per day for 2-3 days.  2 g of P. niguran are macerated. Pills are prepared fruit of P. niguran and the macerated leaves of Cynodon dactylon are macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2-3 days.			drons of oil prepared from seeds of Brassica campest-		
applied to fractured macetace with 2-3 ages of Coth, A fresh mixture is applied and bandaged for a week.  Roots of Pergularia demina are macerated with 2-3 seeds of P. nigrum L. Pills are made from the macerated mixed by a proper of Pergularia demina are macerated and mixed with 1 powdered P. nigrum fruit. From the mixture, pills are prepared. One pill is taken three times per day for 2-3 days.  2 of Windom Indople leaves of Polygoum hydropie leaves of Cynodom dactylon are macerated. A piper, 1 nat of Myristate frograms. I fruit of Terminalia chebula, 3g carum cavi, 20 g young leaves of Cynodom dactylon are macerated. Pills are prepared from the mixture. I pill is taken with 1 cup of water thrice daily for 2 weeks.  1 powdered fruit of P. nigrum and the macerated leaves of Polygoum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2-3 days.  Catarrh with cough			ric are mixed and macerated. The mixture is then		
and bandaged for a week.  Roots of Perguinar dadenia are macerated with 2-3  Roots of Perguinar dadenia are macerated with 2-3  Roots of Perguinar dadenia are macerated with 2-3  seeds of Perguinar deamic are macerated with 2-3  seeds of Perguinar deamic are macerated with 2-3  seeds of Perguinar deamic are macerated in mediately.  2.5 g. nigum. L. Pils are made from the mixture, polygonum hydropiper leaves are macerated and mixed with 1 powdered P. nigum fult. From the mixture, palls are prepared. One pill is taken three times per day for 2-3 days.  2 g of P. nigum. 1 handful leaves of Polygonum hydrophyper leaves of Polygonum hydropiper leaves of Polygonum hydrophyper leaves of Polygonum hydrophyper leaves of Cynodon dactylon are macerated. Pills are prepared from the mixture. I pill is taken with 1 cup of water thrice daily for 2 weeks.  1 powdered fruit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2-3 days.  Catarrh with cough					
ared bandagaed for a week.  Roots of Pergularia daemia are macerated with 2–3 seeds of P. nigrum I. Pills are made from the macerated with 2–3 ated mix are taken thrice daily administered immediately. 2.5 g P. nigrum, I powdered P. nigrum in the times per with 1 powdered P. nigrum, I powdered P. nigrum in the times per with 1 powdered P. nigrum in the times per with 1 powdered P. nigrum in the times per pepared. One pill is taken three times per pills are prepared from the mixture. I pill is taken with 1 cup of water thrice daily for 2 weeks.  I powdered fruit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. I is taken three times daily for 2 weeks.  I powdered fruit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2 weeks.  I powdered fruit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2–3 days.					
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Roots of <i>Pergularia deemina</i> are macerated with 2-3 ated 56 etc. In the macerated seeds of P. nigrum L. Pills are made from the macerated and with a retaken thrice daily administered immediately.  2.5 g P. nigrum fuilts and 3 g Datura metel L. root are ground. It is orally administered immediately. Polygonum hydropier leaves an emacerated and mixed with 1 powdered P. nigrum, 1 handful leaves of Polygonum hydroper, 1 nut of Myristica fragrans, 1 fruit of piper, 1 nut of Myristica fragrans, 1 fruit of leaves of Ground or dacylon are macerated. Pills are prepared from the mixture. I pill is taken with 1 cup of water thrice daily for 2 weeks.  1 powdered fruit of P. nigrum and the macerated leaves of Orlogonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2-3 days.  2 catarrh with cough			and bandaged for a week.		
seeds of <i>P. nigrum</i> L. Pills are made from the macerated and mix are taken thrice daily 2.5 g / nigrum fuits and 3 g datum and 4 g datum and 4 g datum 4 datum and 4 g da		Seed	Roots of <i>Pergularia daemia</i> are macerated with 2–3	Irregular menstruation	Hasan et al. 2012
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2.5 g. nigrum fruits and 3 g Datura metel L. root are ground. It is orally administered immediately.  Polygonum hydropiper leaves are macerated and mixed with 1 glowdered by nigrum fruit. From the mixture, pills are prepared. One pill is taken three times per day for 2–3 days.  2 g of P. nigrum, 1 handful leaves of Polygonum hydropipera, 1 nut of Myristica fragrans, 1 fruit of permitted replaced from the mixture. I pill is taken with 1 cup of water thrice daily for 2 weeks.  1 powdered fruit of P. nigrum and the macerated leaves of Polygonum hydropiper are mixed. Pills are prepared from the mixture. It is taken three times daily for 2–3 days.  Catarrh with cough			ated mix are taken thrice daily		
ground. It is orally administered immediately.  Polygonum hydropiper leaves are macerated and mixed with 1 powdered P. nigrum fruit. From the mixture, pills are prepared. One pill is taken three times per day for 2-3 days. 2 g of P. nigrum, 1 handful leaves of Polygonum hydro- piper., 1 nut of Myristica fragrans, 1 fruit of Terminalia chebula, 3 g Carum carvi, 20 g young leaves of Cynodon dactylon are macerated. Pills are prepared from the mixture. 1 pill is taken with 1 cup of vader thrice daily for 2 weed. Pills are pre- pared from the mixture. It is taken three times daily for 2-3 days.  Catarrh with cough		Fruit	2.5 g <i>P. nigrum</i> fruits and 3 g <i>Datura metel</i> L. root are	Dog bite	Tumpa, Hossain, and Ishika 2014
Polygonum hydropiper leaves are macerated and mixed with 1 powdered <i>P. nigrum</i> fruit. From the mixture, pills are prepared. One pill is taken three times per day for 2–3 days. 2 g of <i>P. nigrum</i> , 1 handful leaves of <i>Polygonum hydro-</i> piper, 1 nut of <i>Myristica fragrans</i> , 1 fruit of Teminalia chebula, 3g Carum carvi, 20g young leaves of Cyndoul actsylon are macerated. Pills are prepared from the mixture. 1 pill is taken with 1 cup of water thrice daily for 2 weeks. 1 powdered fruit of <i>P. nigrum</i> and the macerated leaves of <i>Polygonum hydropiper</i> are mixed. Pills are pre- pared from the mixture. It is taken three times daily for 2–3 days.  Catarrh with cough			ground. It is orally administered immediately.		
with 1 powdered <i>P. nigrum</i> fruit. From the mixture, pills are prepared. One pill is taken three times per day for 2–3 days.  2 g of <i>P. nigrum</i> , 1 handful leaves of <i>Polygonum hydro-piper</i> , 1 nut of <i>Myristica fragrans</i> , 1 fruit of <i>Terminalia chebula</i> , 3 g <i>Carum cani</i> , 20 g young leaves of <i>Cynodon dactylon</i> are macerated. Pills are prepared from the mixture. 1 pill is taken with 1 cup of water thrice daily for 2 weeks.  1 powdered fruit of <i>P. nigrum</i> and the macerated leaves of <i>Polygonum hydropiper</i> are mixed. Pills are prepared from the mixture. It is taken three times daily for 2–3 days.  Catarrh with cough		Fruit	Polygonum hydropiper leaves are macerated and mixed	Menstrual pain	
pills are prepared. One pill is taken three times per day for 2–3 days.  2 g of <i>P. nigrum</i> , 1 handful leaves of <i>Polygonum hydro-piper</i> , 1 nut of <i>Myristica fragrans</i> , 1 fruit of <i>Preminalia chebula</i> , 3 g <i>Carum canvi</i> , 20 g young leaves of <i>Cynodon dactylon</i> are macerated. Pills are prepared from the mixture. 1 pill is taken with 1 cup of water thrice daily for 2 weeks.  1 powdered fruit of <i>P. nigrum</i> and the macerated leaves of <i>Polygonum hydropiper</i> are mixed. Pills are prepared from the mixture. It is taken three times daily for 2–3 days.  Catarrh with cough			with 1 powdered <i>P. niarum</i> fruit. From the mixture.	_	
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or <i>Polygonum nyaropipe</i> r are mixed. Fins are pre- pared from the mixture. It is taken three times daily for 2–3 days.		Fruit		Menstrual pain	
pared from the mixure. It is taken three times dalify for 2–3 days.  Catarrh with cough			or <i>Polygonum nyaropiper</i> are mixed. Pilis are pre-		
iol 2–5 uays. Catarrh with cough			pared from the mixture. It is taken three times daily ومريع ع ع طين		
במנשוון אונון כמהאין		E2	101 2-3 udys.	Catarrh with cough	
		1011		Catallii Witi Codgii	:

in the different types of extracts. The structures of the major chemicals are shown in Figure 3 and their mech-

Table 1. Continued.				
Country	Part of plant used	Mode of preparation/ dosage	Ailments/Medicinal use	References
		12 fruits of <i>P. nigrum</i> , 5g leaves and cord of <i>Solanum</i> sisymbriifolium, 12 leaves of Cinnamomum tamala, 2 fruits of <i>P. lonaum</i> . 5–6 a bark of Cinnamomum zevla-		
		nicum, 5–6 g rock salt and 24 g sugar candy are		
		mixed and boiled in 500 mL of water in a clay pot.		
		When it forms 1 cup it is filtered after cooling. The		
		warm solution is taken once a daily for 1 week.		
Cambodia	Seed	Crushed	Liver diseases	Chassagne et al. 2017
Thailand	Fruit	Decoction	Treating numbness	Neamsuvan et al. 2015
Pakistan	Seed	Powder	Fever	Shah and Rahim 2017
	Fruit	Powder	Body pain	
	Seed	Juice of the leaves of Solanum surattense along with	Joint pain	Dey and De 2012
		the seed powder <i>P. nigrum</i> is orally taken.		
Philippines	Leaf	Decoction or infusion	Toothache	Abe and Ohtani 2013
Malaysia	Fruit	Z	Cough	Mohamad et al. 2011
Mexico	Z	Z	Mouth diseases, gastrointes-	Sharma et al. 2017
			tinal disorders	
	Leaves	Infusion, Mouthwash	Dental caries, gum disease	Rosas-Pinon et al. 2012
Poland	Leaves	Infusion	Digestive problems	Kujawska and Hilgert 2014
Mauritius	Z	A juice is prepared with 3 leaves of Mormodica charan-	Type 2 Diabetes	Mootoosamy and Fawzi 2014
		tia L. together with <i>P. nigrum</i> and is consumed once		
		טבו איפפא.		
Algeria	Seed	Intusion, powder, catapiasm	Lower blood glucose level	relli, Eshauit, and Ould El Hadj Khelil 2016
Morocco	Z	Dried plants of Bunium bulbocastanum, Capparis spinosa, Marietica francas Systaina promaticum, P. nigrum, P.	General health, gynaecological,	Teixidor-Toneu et al. 2016
		longum, P. cubeba, Rosa centrifolia, Illicium verum,		
		Asphodelus microcarpus, Alpinia officinarum and		
		Lingiber officinale are ground and mixed with food.		

NI: Not indicated.

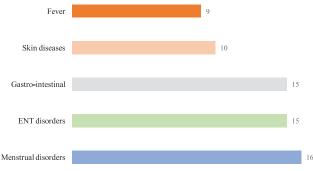


Figure 2. Top 5 most reported disorders using itional medicine.

anisms of action are displayed in Figure 4. Phytochemical screening of P. nigrum fruit extracts (water, methanol, and ethanol) revealed the presence of a range of secondary metabolites, including alkaloids, glycosides, terpenoids, steroids, flavonoids, tannins, and anthraquinones (Nahak and Sahu 2011). The main odorants identified from the fruit of P. nigrum were  $\alpha$ - and  $\beta$ -pinene, myrcene,  $\alpha$ -phellandrene, limonene, linalool, methylpropanal, 2- and 3-methylbutanal, butyric acid and 3-methylbutyric acid (Jagella Grosch 1999).

The first phytochemical report of P. nigrum essential oil was carried out by (Pino et al. 1990), whereby a total of 46 components was detected using gas chromatography-mass spectrometry (GC/MS) including (E)-B-ocimene, 6-guaiene, (Z) (E)-farnesol, 6-cadinol, and guaiol. Another phytochemical analysis conducted by (Kapoor et al. 2009) compared the essential oil, and the ethanol and ethyl acetate oleoresins of P. nigrum fruits using Clevenger and Soxhlet apparatus, respectively. GC-MS analysis showed a total of 54 compounds with the major component being  $\beta$ -Caryophyllene (29.9%) together with limonene (13.2%),  $\beta$ -pinene (7.9%), sabinene (5.9%), and some other components in lower amounts. In contrast, Tchoumbougnang et al. (2009) found different levels of compounds in the fruit oil;  $\delta$ -3-carene (18.5%), limonene (14.7%),  $\beta$ -caryophyllene (12.8%), and sabinene (11.2%) as major components. Additionally, Orav et al. (2004) found that the fruit oil principally contained (E)- $\beta$ -caryophyllene (1.4–70.4%), eugenol (0.1–41.0%), lim-(2.9-38.4%), $\beta$ -pinene (0.7–25.6%), onene 3-carene (1.7-19.0%), sabinene (0-12.2%), and  $\alpha$ -pinene (0.3-10.4%). Similarly, caryophyllene (23.98%), limonene (14.36%), and  $\alpha$ -terpinene (13.26%) are the main compounds identified in the essential oil, as analyzed by (Jeena et al. 2014). Moreover, Wang et al. (2018) analyzed 23 P. nigrum oil samples from various countries including Malaysia, Sri Lanka, Madagascar, Ecuador, India, Vietnam, Indonesia, Brazil, India, and China. The dominant terpenes in all of the oil samples were  $\beta$ -caryophyllene (14.7–52.5%), 3-carene (0.8-21.1%), limonene (4.4-18.7%),  $\alpha$ -pinene (1.5-7.3%), and  $\beta$ -pinene (1.7–9.4%). Also, sabinene was present in many samples (1.0-15.9%) but in trace amount in the Chinese and Malaysian samples (< 0.2%).

On the other hand, in the ethanol and ethyl acetate oleoresins, the key component was found to be piperine (63.9 and 39.0%) along with various other components in

smaller quantities. In other phytochemical analyses on P. nigrum fruits ethanolic extracts, piperine was also found to be the active major compound (Singh et al. 2013; Zarai et al. 2013). Also, Singh et al. (2004) observed that the acetone extract also showed the presence of piperine (33.53%) as the major component, followed by piperolein B (13.73%), an alkaloid of MW 361 (5.59%) and its isomer (5.49%), piperamide (3.43%), piperettine (2.76%), quineensine (3.23%), hinokinin (1.88%), retrofractamide A (1.57%), and N-trans feruloyltyramine (1.45%). Moreover, Liu et al. (2013) determined the phytochemical profile of the berries of five different genotypes of P. nigrum in China, namely: Jianyin-1, Banyin-1, Banyin-2, Banyin-3, and Banyin-4. The piperine content of the five genotypes ranged from 3.12 to 5.78%. Banyin-1 genotype was found to contain higher levels of  $\alpha$ -thujene,  $\beta$ -pinene, 3-carene, limonene, and caryophyllene compared to the other tested samples.

Moreover, the petroleum ether extract of P. nigrum dried whole fruits was found to contain the compounds: stigmastanol,  $\beta$ -sitosterol, stigmasterol, stigmastanol 3-O- $\beta$ -D-glucopyranoside,  $\beta$ -sitosterol 3-O- $\beta$ -D-glucopyranoside, [(2E, 4E)octadienoyl]-N-isobutylamide, sarmentine, [(2E,4E)- dodecadienoyl]-N-isobutylamide, [(2E,4E)-dodecadienoyl]pyrrolidine, hexadecenoic ethyl ester, octadecanoic acid, pellitorine, hexadecanoylpyrrolidine, [(2E)-octadecanoyl] pyrrolidine, 1-[(2E,4E,12Z)-octadecatrienoyl]-N-isobutylamide, piptaline, 1-[7-(3,4-methylenedioxyphenyl)-(2E,4E)-heptadienoyl]-N-isobutylamide, 1-(3,4-methylenedioxyphenyl)-(1E)-tetradecene (Siddiqui et al. 2004).

Three amides, pipgulzarine, pipzorine, and piptahsine, were also identified in the dried seeds of P. nigrum using petroleum ether extraction along with nine known constituents including (2E,4E,8Z)-N-(isobutyl) eicosatrienamide, pellitorine, pipercide, piperine, stigmastanol, stigmasterol, decurrenal, stigmasterol 3-O- $\beta$ -D-glucopyranoside, 5,10(15)-cadinen-4-ol (Siddiqui et al. 2003). In addition, the crystalline compound [{(1,5-(1,3)-benzodioxol-5yl)-1-oxo-2,4 pentadienyl}-piperidine] was also isolated from the petroleum ether extract of P. nigrum seeds along with fifteen sesquiterpenes (linalool, 4-terpinol,  $\alpha$ -terpinol,  $\delta$ -elemene,  $\alpha$ -copane,  $\beta$ -elemene,  $\beta$ -caryophyllene,  $\alpha$ -caryophyllene, gurjunene,  $\beta$ -bisabolene,  $\delta$ -cadinene, elemol, caryophyllene oxide, murrolene,  $\beta$ -eudesmol) (Gupta, Gupta, and Gupta 2013).

Lim et al. (2009) identified the alkaloids piperdine, pelliterine, piperidine, piperine, and pellitorine in P. nigrum dried roots from Malaysia. In addition, seven alkaloids, N-isobutyl-4-hexanoyl-4-hydroxypyrrolidin-1-one, erythro-1-(1-oxo-4,5-dihydroxy-2E-decaenyl)piperidine, threo-1-(1-oxo-4,5-dihydroxy-2E-decaenyl) piperidine, threo-N-isobutyl-4,5-dihydroxy-2E-octaenamide, 1-(1,6dioxo-2E,4E-decadienyl) piperidine, 1-[1-oxo-3(3,4-methylenedioxy-5-methoxyphenyl)-2Z-propenyl]piperidine, and 1-[1-oxo-5(3,4-methylenedioxyphenyl)-2Z,4E-pentadienyl] pyrrolidine, were isolated from the roots of P. nigrum (Wei et al. 2004).

**Table 2.** Ethnoveterinary properties of *P. nigrum*.

Country	Part of plant used	Mode of preparation/dosage	Ailments/ Medicinal use	References
India	Seed	Equal quantity of <i>P. nigrum</i> , hengu ( <i>Ferula asafetida</i> ), ginger, turmeric and common salt are mixed and	Anthrax, Constipation, Bloating	Usha, Rajasekaran, and Siva 2016
	NI	orally fed to cattle.  One handful of the crushed leaves of Allium sativum,  Tylophora indica, Datura metel, Aegle marmelos and 10–15 P. nigrum are mixed with 2 spoons of mustard. Ragi balls along with this paste is orally taken	Loss of appetite	Naik et al. 2012
	NI	twice a day for 4 days.  10 <i>P. nigrum</i> are mixed with 5 inches of <i>Tenospora cordifolia</i> stem with 80 mL of Aloe <i>barbadensis</i> is added to 4 betel leaves, 1 <i>Allium sativum</i> and <i>Allium cepa</i> ground with a cup of water. The mixture is given	Cough	
	NI	orally two times daily for 3 days.  10 g P. nigrum, 15 leaves of Adhatoda vasica, 15 leaves of Tylophora indica, 1 handful of Albizia amera, 1 or 2 leaves of Aloe barbadensis, 1 Allium sativum and 100 g cherry are ground to a decoction and is fed twice daily.	Cough	
	Seed	Seeds of <i>P. nigrum</i> L., leaves of <i>Acalypha indica</i> L. and <i>Leucas aspera</i> (Willd.) Link and bulb of <i>Allium cepa</i> L. are crushed and given to animals.	Black quarter disease	Seebaluck, Gurib-Fakim, and Mahomoodally 2015
	Seed	Orally given to camels	Snake bite	Sharma and Manhas 2015
	Seed	Equal proportions of seed powder of <i>P. nigrum, F. asafetida</i> , ginger, turmeric powder and table salt are mixed and fed with rice gruel.	Indigestion	Mallik, Panda, and Padhy 2012
	Seed	A paste is made 10–15 <i>P. nigrum</i> seeds, 50 g ginger, 50 g garlic and butter and divided into two equal halves. Half is orally given to the animal and the other half is applied together over.	Cough and cold	
	Flowers	The ground fruit of Capsicum annuum is mixed with flowers of Syzygium aromaticum and P. nigrum in water and given orally.	Skin disease of livestock	Meghvansi et al. 2010
	Fruit	P. nigrum fruit, seeds of Trachyspermum ammi, rhizome of Zingiber officinale and Ferula asafetida are mixed and crushed with water and the paste is adminis- tered to affected area.	Blot	Phondani, Maikhuri, and Kala 2010
	NI	Powders of <i>P. nigrum</i> mixed with water and added to drink.	Poisoning	
	NI	Ground <i>P. nigrum</i> is mixed with water and black salt.  Mixture is added to feed.	Indigestion	
	NI	P. nigrum, seeds of Trachyspermum ammi, rhizome of Curcuma domestica, leaves of Trigonella foenum and Dendrocalamus strictus are ground and added to drink.	Pneumonia	
	NI	One teaspoon of root juice of <i>Clitoria ternatea</i> Linn. along with a <i>P. nigrum</i> Linn. for 20 days.	Infertility	Ghosh 2008
	NI	One teaspoon of root juice of <i>Mimosa pudica</i> Linn. along with <i>P. nigrum</i> Linn. for 20 days.	Infertility	
	Fruit	5 g of fruit powder of <i>P. nigrum</i> Linn. is mixed in a cup of lukewarm water and drunk at night.	Constipation	
	NI C. I	The roots of <i>Hemidesmus indicus</i> Linn. are ground with <i>P. nigrum</i> and is orally taken.	Stomach ulcers	Rajith and Ramachandran 2010
	Seed	The dried <i>P. nigrum</i> seed paste and rock salt are mixed with curd and is fed orally.	Lack of appetite	Jayakumar et al. 2017
	Seed Seed	The seeds of <i>P. nigrum</i> are boiled in water and the extract is fed orally.  The seed powder of <i>P. nigrum</i> is mixed with rock salt	Bloating Cold	
	Seed	and jaggery and fed orally.  The seed powder of <i>P. nigrum</i> is mixed with alcohol	Cold	
	Seed	and orally fed.  The seed powder of <i>P. nigrum</i> is mixed with rock salt	Constipation	
	Seed	and jaggery and is fed orally.  The paste of the seeds is made with rock salt and curd	Constipation	
	Seed	and is orally fed.  A paste of <i>P. nigrum</i> seeds and seeds of <i>Cuminum cyminum</i> , <i>Carum bulbsocastanum</i> , <i>Ferula assa-foetida</i> , <i>P. longum</i> , and <i>Trachyspermum roxburghianum</i> , and the	Constipation	
	Seed	rhizome of Zingiber officinale in equal proportion are mixed with rock salt and fed orally.  The seeds paste of the P. nigrum, Cuminum cyminum, Carum bulbsocastanum, Ferula assa-foetida, P. longum, Trachyspermum roxburghianum, rhizome of Zingiber officinale mixed in equal portion along with rock salt is fed to the animals.	Diarrhoea	

Country	Part of plant used	Mode of preparation/dosage	Ailments/ Medicinal use	References
	Seed	Crushed <i>P. nigrum</i> seeds are made to a paste with rock salt and curd, and the paste is given orally.	Diarrhoea	
	Seed	The seeds powder is mixed with rock salt and jaggery and is given orally.	Diarrhoea	
	Seed	The seeds paste is mixed with boiled rice and is given orally.	Diarrhoea	
	Seed	A paste is prepared with the seeds of <i>P. nigrum</i> , <i>Cuminum cyminum</i> , <i>Carum bulbsocastanum</i> , <i>Ferula assa-foetida</i> , <i>P. longum</i> , <i>Trachyspermum roxburghia-num</i> , rhizome of <i>Zingiber officinale</i> . The paste is mixed in equal amount with rock salt and is given orally.	Ecto-parasitic infection	
	Seed	A paste is made using crushed <i>P. nigrum</i> seeds, rock salt and curd and is given orally.	Ecto-parasitic infection	
	Seed	A paste is made with crushed <i>P. nigrum</i> seeds, rock salt and curd and is given orally.	Endo-parasitic infection	
	Seed	A paste is prepared using equal amount of crushed seeds of Cuminum cyminum, Carum bulbsocastanum, Ferula assa-foetida, P. longum, Trachyspermum roxburghianum, rhizome of Zingiber officinale and is mixed with rock salt and is orally fed.	Endo-parasitic infection	
	Seed	Equal amount of seeds of <i>P. nigrum, Cuminum cyminum, Carum bulbsocastanum, Ferula assa-foetida, P. lon-gum,</i> Trachyspermum roxburghianum and rhizome of <i>Zingiber officinale</i> are made to a paste and is mixed in equal amount with rock salt is given orally fed.	Indigestion	
	Seed	Crushed dried <i>P. nigrum</i> seeds are made to a paste with rock salt and curd and is given orally.	Indigestion	
	Seed	P. nigrum seeds are crushed and is mixed with rock salt and jaggery and is given orally	Indigestion	
	Seed	The seeds paste of the Cuminum cyminum, Carum bulb- socastanum, Ferula assa-foetida, P. longum, Trachyspermum roxburghianum, rhizome of Zingiber officinale mixed in equal portion along with rock salt is given orally.	Flatulence	
	Seed	P. nigrum seed powder mixed with rock salt is given along with fodder.	Musth	
	Seed	P. nigrum seeds, seeds of Cuminum cyminum, Carum bulbsocastanum, Ferula assa-foetida, P. longum, Trachyspermum roxburghianum, rhizome of Zingiber officinale are made to a paste and are mixed in equal proportion with rock salt and is given orally.	Stomach ache	
Pakistan	Fruit	P. nigrum fruit is placed inside the cake of dough and fed to the infected goat.	Skin infection	Aziz et al. 2018
	Seed	50 g of seeds of <i>P. nigrum</i> L., <i>Amomum subulatum</i> Roxb, <i>Foeniculum vulgare</i> Mill and <i>Cinnamomum</i> are mixed in jaggery and administered <i>per os</i> in 4 equal doses in 4 days.	Genital proloapse	Dilshad et al. 2008
	Fruit	50–100 g of <i>P. nigrum</i> fruit is given in a drench ball.	Anthelmintic	Jabbar et al. 2006
angladesh	Seed	The leaves of <i>Tragia involucrata</i> L. are macerated with seeds of <i>P. nigrum</i> L. and fed to cattle	Badla disease in cattle	Rahmatullah et al. 2013
	Seed	The roots of <i>Physalis micrantha</i> Link are macerated with two seeds of <i>P. nigrum</i> L. and fed to cattle.	Gastrointestinal disorder in cattle	
thiopia	Leaves	P. nigrum leaves are squeezed to take out fluid and it is drenched to the animals.	Respiratory disease	Assefa and Bahiru 2018

NI: Not indicated.

# Pharmacological properties of P. nigrum

P. nigrum and its bioactive compounds were also found to possess other important pharmacological properties including antimicrobial, antioxidant, anticancer, analgesic, anticonvulsant, neuroprotective, hypoglycemic, hypolipidemic, and anti-inflammatory activities (see detailed findings in Table 3).

# **Antimicrobial properties**

The emergence and prevalence of drug-resistant pathogenic microorganisms has led to a decline in the efficacy of traditional antimicrobial therapy. Consequently, treatment of infections is becoming progressively more challenging. To address this emerging issue, it is essential that novel therapies be developed to spare existing broad-spectrum antimicrobials including antibiotics (Spaulding et al. 2018).

Antimicrobial efficacy of P. nigrum have been reported against a broad range of pathogens (see Table 4). Depending on the tested concentration and different solvents used for P. nigrum extraction, the susceptibility of the microorganisms was found to vary among studies. For instance, among several solvent extracts (cold water, hot water, and methanol) of P. nigrum fruit, Khan et al. (2013) found that the cold-water extract had the maximum zone of inhibition

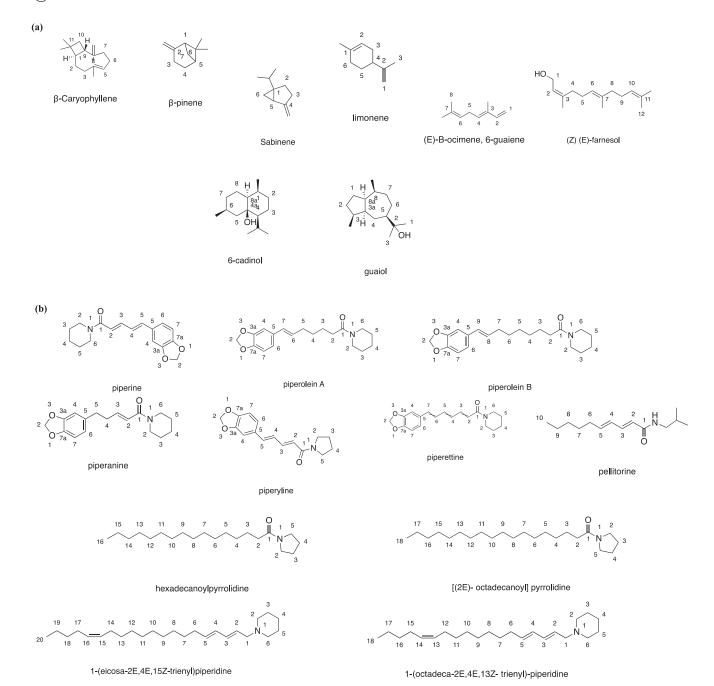


Figure 3. Chemical structures of the compounds identified in P. nigrum (seed, fruit and root) (a) Terpene (b) Alkaloid (c) Amide (d) Sterol and fatty acid.

(ZOI) against *E. coli* (ZOI = 23 mm) while the hot water extract showed maximum ZOI against *S. typhi* and *S. aureus* (ZOI = 22 mm). Besides, the methanolic extract showed the highest inhibition against *E. coli*, *S. typhi* and *P. aeruginosa* (ZOI = 21mm), nonetheless, did not affect *S. aureus*. Another study (Karsha and Lakshmi 2010) observed that the acetone extract was more active than the dichloromethane extract against several bacteria among which, *S. aureus* was inhibited to the greatest extent (ZOI = 20 mm). Also, the methanolic extract was found to be effective against several phytopathogenic fungi showing highest inhibition on *Puccinia recondite* (Park et al. 2008).

Furthermore, among different solvent extracts of the seed (hexane, dichloromethane, ethanol, and aqueous), the

dichloromethane extract displayed the highest activity against the bacteria *S. aureus*, *E. coli*, *S. typhi*, and *B. subtilis* (Gupta et al. 2014a). Another study by Penecilla and Magno (2011) found that n-Hexane solvent displayed no inhibition against *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*. In contrast, the acetone and ethanol extract were able to inhibit *S. aureus* and *B. subtilis*. The aqueous extract was the most effective, inhibiting *S. aureus* (ZOI = 10 mm), *B. subtilis* (ZOI = 9 mm), and *P. aeruginosa* (ZOI = 13 mm). Several solvent leaf extracts have also been tested for its antimicrobial activity (Akthar, Birhanu, and Demisse 2014; Shanmugapriya et al. 2012). Paulkumar et al. (2014) observed that silver nanoparticles from the aqueous extract of the leaf were more effective against both *Citrobacter* 

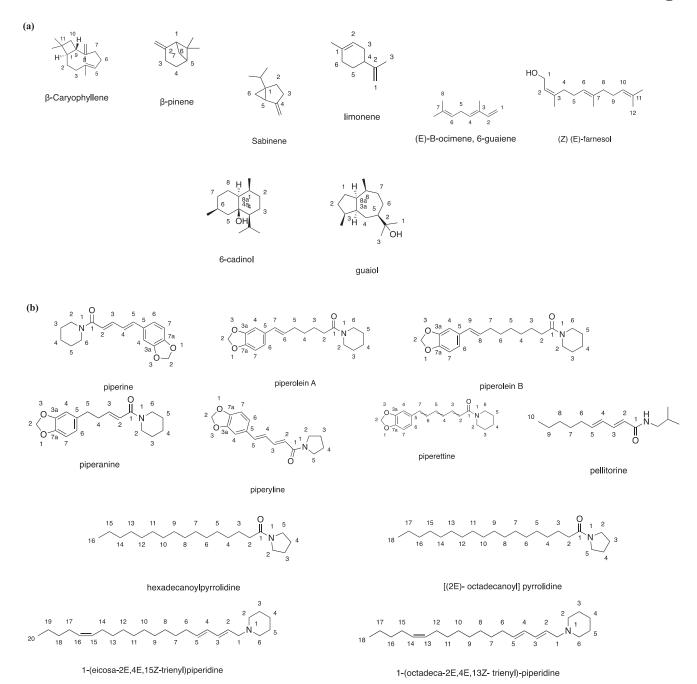


Figure 3. Continued

freundii and Erwinia cacticida (ZOI = 8.962 and 9.052 mm, respectively) than the silver nanoparticles synthesized from *P. nigrum* stem (ZOI = 8.894 and 9.012 mm, respectively).

With regards to the bioactive compounds in *P. nigrum*, two phenolic compounds, 3,4-dihydroxyphenyl ethanol glucoside (A) and 3,4-dihydroxy-6-(N-ethylamino) benzamide (B), were found to inhibit the growth of foodborne pathogens including *S. aureus*, *B. cereus*, *E. coli*, and *S. typhimurium* (with the exception of compound A for the latter bacterium). In general, compound A (MIC = 2.25 mmol/L) was more effective than compound B (MIC = 7.6 mmol/L) but less effective than the positive control, 4-methylcatechol (MIC = 2 mmol/L). Moreover, a combination of piperine with ciprofloxacin significantly reduced the MICs and

mutation prevention concentration of ciprofloxacin against *S. aureus*, including its methicillin-resistant strain. The presence of piperine resulted in an enhanced accumulation and a decrease in ethidium bromide efflux in the wild-type and mutant (CIP $^{\rm r}$ -1) strains, thereby suggesting its role in the inhibition of bacterial efflux pumps (Khan et al. 2013). In addition, a study by (Zarai et al. 2013), they found that piperic acid (MIC in the range  $78.12\text{--}625\,\mu\text{g/mL})$  showed higher antibacterial activity than piperine (MIC in the range  $312.5\text{--}625\,\mu\text{g/mL})$  against many Gram-positive and Gramnegative bacteria.

Biofilm formation is known to play a significant role in the pathogenesis of bacteria. Biofilm development is based on the signal-mediated quorum sensing (QS) system, and

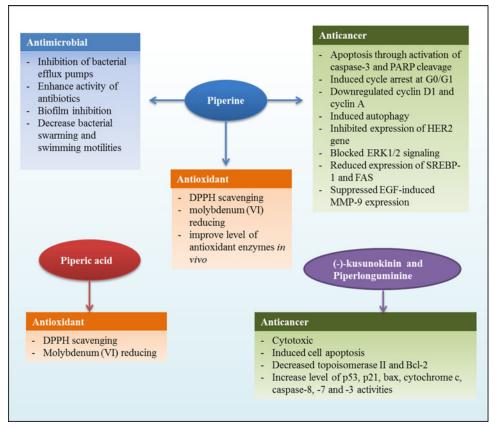


Figure 4. Mechanism of action of mostly studied pharmacological properties of bioactive compounds in P. nigrum.

therefore, interference with QS may prevent biofilm formation and further infections. Singh et al. (2016) investigated P. nigrum extract for its anti-QS potential in inhibiting the formation of biofilm in Cronobacter sakazakii strains. The extract, at a concentration of 100 ppm, caused a 78% reduction in violacein and blue-green color production in both biosensor strains used (Chromobacterium violaceum 026 and Agrobacterium tumefaciens NTL4 (pZLR4)). The extract also caused 60-72% inhibition of biofilm formation in C. sakazakii strains. Also, piperine displayed a minimum biofilm inhibitory concentration (MBIC) of 0.0407 mg/mL against S. mutans. At optical density  $OD_{492} < 0.5$ , the MBIC of both compounds caused significant inhibition of biofilm formation of all the 18 tested strong biofilm-forming isolates (Dwivedi and Singh 2016).

Additionally, Dusane et al. (2014) found that sub-inhibitory concentrations of piperine (0.5-5 μg/mL) decreased bacterial swarming and swimming motilities but increased biofilm formation. At first instance, an increase in biofilm formation seems to be a disadvantage in a therapeutic context, but it should be highlighted that this effect was accompanied by a significant decrease in motility which is known to decrease the spread of infection. In addition, qRTPCR revealed a decrease in the expression of the flagellar gene (fliC) and motility genes (motA and motB) together with an increase in the expression of adhesin genes (fimA, papA, uvrY). More importantly, piperine increased the penetration of both ciprofloxacin and azithromycin into the biofilms of E. coli CFT073, and hence enhanced the ability of these antibiotics to disperse pre-established biofilms.

# **Antioxidant**

Several in vitro assays based on different mechanism have been performed to assess the antioxidant power of P. nigrum. Gulcin (2005) found that the aqueous extract of the seed possesses higher scavenging activity than the ethanol extract against DPPH, superoxide anion, hydrogen peroxide, and total antioxidant activity based on the thiocyanate method, while the latter showed higher ferric reducing power. The variation on antioxidant power of different extracts and fractions of the fruits was also observed by (Nahak and Sahu 2011; Singh et al. 2008). Also, Shanmugapriya et al. (2012) determined the antioxidant power of P. nigrum leaf was also assessed using a number of assays. Among three solvent extracts (ethyl acetate, acetone, and aqueous), the ethyl acetate extract showed the highest DPPH, ABTS, and superoxide anion scavenging effects while the acetone extract exhibited the highest inhibition against hydrogen peroxide, nitric oxide, and was most effective in the phosphomolybdenum assay. On the other hand, the aqueous extract was the strongest ferric reducer.

The essential oil of the fruits also showed more potent inhibitory effects in DPPH, FRAP, and lipid peroxidation assays compared to the ethyl acetate and ethanol oleoresin (Kapoor et al. 2009). Bagheri, Abdul Manap, and Solati (2014) evaluated the DPPH scavenging property of the essential of the seed using two different extraction techniques. They found that the essential oil extract obtained from supercritical-CO<sub>2</sub> extraction showed higher activity (EC<sub>50</sub> =  $103.28 \,\mu g/mL$ ) than that of hydro-distillation (EC<sub>50</sub> =

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Activity	Model used	Plant Part	Extract	Assay	Findings	References
Antioxidant	In vitro	Seed	Aqueous Ethanol	DPPH scavenging Superoxide anion radical scavenging activity Total antioxidant activity determination (Thiocyanate method)	Aqueous: 55% inhibition at 75 µg/mL Ethanol: 48% inhibition at 75 µg/mL Aqueous: 64.2% inhibition at 75 µg/mL Ethanol: 22.6% inhibition at 75 µg/mL Aqueous: 95.5% inhibition at 75 µg/mL Ethanol: 93.3% inhibition at 75 µg/mL Ethanol: 93.3% inhibition at 75 µg/mL Aqueous: 06.55 µg/ml Aqueous: 96.55 µg/ml	Gulcin 2005
				rnar Hydrogen peroxide scavenging	Addedus, 0.803 influbition at 75 µg/mL Ethanol: 0.855 inhibition at 75 µg/mL Aqueous: 83% inhibition at 75 µg/mL Ethanol: 63%, inhibition at 75 µg/mL	
Antioxidant	In vitro	Berries	Phenolic compounds: 3,4-dihy-droxyphenyl ethanol glucoside, 3,4-dihydroxy-6-(N-ethylamino) benzamide Phenolic	DPPH scavenging	EC <sub>50</sub> of 34-dihydroxyphenyl ethanol glucoside, 3,4-dihydroxyphenyl ethanol glucoside, 3,4-dihydroxy-6-(N-ethylamino) benzamide and phenolic acid glycosides were found to be 0.076, 0.27 and 0.12 mg/mL, respectively.	Chatterjee et al. 2007
Antioxidant	In vitro	Fruit	Aqueous Ethanol Methanol	DPPH scavenging	At highest concentration of extract tested (250 µg/mL): Aqueous: 39.92 % inhibition Ethanol: 7461 % inhibition; IC <sub>50</sub> = 14.15 µg/ml Methanol: 63.84 % inhibition	Nahak and Sahu 2011
Antioxidant	In vitro	Berries	Ethanol extract Compounds: Piperine Piperic acid	DPPH	Ethanol: 65.59% inhibition at 50 µg/mL Piperine: 10.28% inhibition at 50 µg/mL Piperine: 10.28% inhibition at 50 µg/mL Piperine acid: 29 5% inhibition at 50 µg/mL	Zarai et al. 2013
				Phosphomolybdenum assay	Ethanoi: 48.2 $\mu$ mol/mL $\alpha$ -tocopherol equivalents) at 25 $\mu$ g/mL Piperine: 58.8 $\mu$ mol/mL $\alpha$ -tocopherol equivalents at 100 $\mu$ g/mL Piperic acid: 64.1 $\mu$ mol/mL $\alpha$ -tocopherol equivalents at 100 $\mu$ g/mL Piperic acid: 64.1 $\mu$ mol/mL $\alpha$ -tocopherol equivalents at 100 $\mu$ g/mL	
Antioxidant	In vitro	Fruit	Essential oil Oleoresins (obtained by extracting with ethanol and ethyl acetate)	DPPH, FRAP, and lipid peroxidation	Inhibitory effect was found in following order: Essential oil > ethyl acetate oleoresin > ethanol oleoresin	Kapoor et al. 2009
Antioxidant Antioxidant	In vitro In vitro	Fruit Seed	Methanol Essential oil	DPPH scavenging DPPH scavenging	$ C_{50}$ = 144.1 $\mu$ g/mL Extracts from supercritical- $CO_2$ and hydrodistillation showed an EC <sub>50</sub> of 103.28 and 316.72 incl'ml resonertively.	Khalaf et al. 2008 Bagheri, Abdul Manap, and Solati 2014
Antioxidant	In vitro	Fruit	Three fractions (R1, R2 and R3) obtained from petroleum ether and and ethyl acetate in the ratio of 6:4, 5:5 and 4:6, respectively.	Linoleic acid peroxidation	At 500 µg/mL of fraction used; R1: 10.21% inhibition R2: 58.89% inhibition R3: 60.48% inhibition	Singh et al. 2008
				DPPH scavenging	At 250 µg/mL of fraction used; R1: 12.41% inhibition R2: 61.24 inhibition R3: 61.11 inhibition	
				Nitric oxide radical scavenging activity	At 100 µg/mL of fraction used; R1: 18.22% inhibition R2: 40.23% inhibition R3: 55.68% inhibition	
				Superoxide anion radical scavenging activity	At 100 µg/mL of fraction used; R1: 18.54% inhibition R2: 62.23% inhibition R3: 70.27%, inhibition	
				Hydroxyl radical scavenging activity	At 1000 µg/mL of fraction used; R1: 21.87% inhibition R2: 61.04% inhibition R3: 63.56% inhibition	
Antioxidant	In vitro	Leaves	Ethyl acetate Acetone Aqueous	DPPH scavenging		Shanmugapriya et al. 2012
						(continued)

Table 3. Other pharmacological properties of P. nigrum.

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Activity	Model used	Plant Part	Extract	Assay	Findings	References
				ABTS radical scavenging	At 100 µg/mL concentration, Ethyl acetate: 84.75% inhibition Acetone: 69.25% inhibition Aqueous: 65.50% inhibition At 100 µg/mL concentration; Ethyl acetate: 72.75% inhibition Acetone: 69.25% inhibition ition Aqueous: 68.96% inhibition	
				Phosphomolybdenum	At 100 µg/mL concentration; Ethyl acetate: 00.76% inhibition Acetone: 00.95% inhibition Acetone: 00.95% inhibition attached the property of th	
				Hydrogen peroxide scaveng- ing activity	At 100 µg/mc concentration; Ethyl acetate: 10.10% inhibition Acetone: 14.40% inhib-	
				Nitric oxide inhibition	tron Aqueous; 00:34% Inhibition At 100 µg/mL concentration; Ethyl acetate: 34.10% inhibition Acetone: 42.80% inhibition Aqueous; 23.40% inhibition	
				Superoxide inhibition	At 100 µg/mL concentration; Ethyl acetate: 58.50% inhibition Acetone: 25.50% inhib-ition Aqueous: 18.30% inhibition	
				FRAP	At 100 µg/mL concentration; Ethyl acetate: 1.113 mg BHT equivalent/g inhibition Acetone: 0.852 mg BHT equivalent/g inhibition Aqueous: 1.256 mg BHT equivalent/g inhibition halpstion	
Antioxidant	In vitro	Peppercorn	50% Acetone 80% methanol	ABTS scavenging	Acetone: 39.8 Trolox equivalent µmol/g Methanol: 23.3 Trolox equivalent µmol/g	Su et al. 2007
				ORAC	Acetone: 395 Trolox equivalent µmol/g Methanol: 363 Trolox equivalent µmol/g	
				FRAP	Acetone: 1.09 disodium ethylenediaminete- traacetate (EDTA) equivalent mg/g Methanol: 0.54 EDTA equivalent mg/g	
				DPPH scavenging	Acetone: $ED_{50}$ Around 1.20 mg/mL Methanol: $ED_{50} = 146 \text{ mg/ml}$	
Antioxidant	In vitro	Z	Essential oil	ABTS scavenging	IC <sub>50</sub> = 223.8 mg/mL	Zhang and Xu 2015
Antioxidant	In vitro	Z	Compound: N-trans-	DPPH scavenging	C <sub>50</sub> = 1333.0 mg/mL EC <sub>50</sub> = 11.82 μg/mL	Tu et al. 2016
Antioxidant	In vitro	Fruit	n-hexane Chloroform Methanol Aqueous	DPPH scavenging	Hexane: $IC_{50}$ = 1830.0 $\mu$ g/mL Chloroform = $IC_{50}$ = 164.9 $\mu$ g/mL	Sruthi and Zachariah 2017
				Phosphomolybdenum method	Methanol = IC <sub>50</sub> = 153.9 μg/mL Aquoeus = IC <sub>50</sub> = 1025.0 μg/mL M AAE. Molar ascorbic acid equivalents/g of extract Hexane: 0.41AAE/g Chloroform: 1.01AAE/g Methanol: 0.73AAE/g Aquoeus: 0.45AAE/g	
				FRAP	M AAE: Molar ascorbic acid equivalents/g of extract Hexane: 0.46 AAE/g Chloroform: 0.55 AAE/g Methanol: 0.52 AAE/g Aqueous: 0.26 AAE/a	
Antioxidant In	In vivo- Male Wistar rats	Pod	Black pepper powder (0.25 g/kg body weight in water p.o) and piperine (0.02 g/kg body weight in water, p.o)	ı	Reduced thiobarbituric acid reactive substances (TBARS) and conjugated dienes (CD) levels Maintained the level of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), glutathione-S-	Vijayakumar, Surya, and Nalini 2004

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	Vijayakumar and Nalini2006	Hritcu et al. 2014	Jeena et al. 2014	Sriwiriyajan et al. 2017		Ee et al. 2009		Li et al. 2011	Motiwala and Rangari2015	Selvendiran, Prince Vijeya Singh, and Sakthisekaran2006	Ouyang et al. 2013	Do et al. 2013	Sriwiriyajan et al. 2014	Pradeep and Kuttan 2002	(continued)
transferace (CCT) are traduced duta-	V.	spa- ion of		1.18 µg/ nL N-620:	After 72 h of exposure; MCF-7: IC <sub>50</sub> = 1.63 μg/mL MDA-MB-231: IC <sub>50</sub> = 71.54 μg/ mL MDA-MB-468: IC <sub>50</sub> = 2.19 μg/mL SW- 620: IC <sub>60</sub> = 4.62 μg/mL	osure: Chloroform : $IC_{50} =$ roleum ether: $IC_{50} =$	IC <sub>50</sub> = 1.8 μg/mL IC <sub>50</sub> = 13 μg/mL	glycoprotein, multidrug otein 1 (MRP1) and breast ince protein (BCRP) depend- oresistant cancer cells	W	Suppressed benzo(a)pyrene (B(a)p) induced Sel- lung cancer in mice by decreasing the levels of total protein and protein bound carbohydrate components (hexose, hexos- amine and sialic acid)	aP: IC <sub>50</sub> = 74.4μΜ 1 PC-3:	;; SKBR3: $IC_{50} = 50  \mu M$ 00 $\mu M$	MCF- IC <sub>50</sub> =	Dichloromethane extract: $MC_{F-7}$ : $K_{Co} = 23.46 \mu g/mL$ $MDA-MB-468$ : $K_{Co} = 7.94 \mu g/mL$ $MDA-MB-231$ : $K_{Co} = 38.82 \mu g/mL$ Administration of piperine caused a 95.2% Prareduction in tumor nodule formation.	
	ı	ı		MTT assay Breast cancer cell lines (MCF-7, MDA-MB-231 and MDA- MB-468) Colorectal cancer cell line (SW-620)		MTT assay Human myeloid leukemia (HL-60 cell)	MCF-7 HeLa	MTT assay Doxorubicin resistant MCF-7 and A-549	MTT assay MCF-7 cell	ı	MTS assay Human prostate cancer cell lines (LNCaP, PC-3 and DU145)	MTT assay HER2-overexpressing breast cancer cells (SKBR3 and MCF-7 cell)	MTT assay Breast cancer MCF-7, MDA-MB-468 and MDA-MB-231 cell lines	1	
	Piperine (40 mg/kg body weight) in 1% carboxymethyl cellu- lose, p.o	Methanol	Essential oil	Compound: (-)-kusunokinin	Compound: piperlonguminine	Chloroform and petroleum ether extract	Pellitorine	Compound: Piperine	Compound: Piperine	Compound: Piperine (50 mg/kg body weight)	Compound: Piperine	Compound : Piperine	Methanol and dichloromethane	Compound: Piperine	
	Z	Fruit	Fruit	Fruit		Root		Z	Z	I	I	I	Fruit	Ē	
	<i>In vivo</i> -Male Wistar rats	In vivo-Male Wistar rasts	<i>In vivo</i> -Balb/C mice	In vitro		In vitro		In vitro	In vitro	<i>In vivo</i> - male Swiss albino mice	In vitro-	In vitro	In vitro	In vivo- C57BL/6 mice	
	Antioxidant	Antioxidant	Antioxidant	Anticancer		Anticancer		Anticancer	Anticancer	Anticancer	Anticancer	Anticancer	Anticancer	Anticancer	

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Activity	Model used	Plant Part	Extract	Assay	Findings	References
	In vitro			MTT assay B16F-10 melanoma cells	reduction in serum sialic acid level and serum gamma glutamyl transpeptidase activity.  At 100 µg/mL concentration after 48 h, piperine was 100% cytotoxic to B16F-10 cells	
Anticancer	In vitro	Fruit	50% ethanol	MTT assay Colorectal cancer cell lines (HT-29, HCT-116, and HCT-15)	After 72 h exposure; HCT-116: $(C_{50} = 3.4 \mu\text{g})$ mL HCT-15: $(C_{50} = 1.9 \mu\text{g}/\text{mL HT-29}$ : $(C_{50} = 7.4 \mu\text{g}/\text{m})$	Prashant et al. 2017
Anticancer	In vitro	Fruit	Piperine free <i>P. nigrum</i> extract	MTT assay against various cancer cell lines	/ 4 Hg/mL MCF-7: IC <sub>50</sub> = 7.45 µg/mL MDA-MB-231: IC <sub>50</sub> = 2.267 µg/mL MDA-MB468: IC <sub>50</sub> = 18.19 µg/mL ZR75-1: IC <sub>50</sub> = 13.85 µg/mL HT-29: IC <sub>50</sub> = 27.74 µg/mL SW-620: IC <sub>50</sub> = 29.56 µg/mL H-358: IC <sub>50</sub> = 34.69 µg/ml A-549: IC <sub>50</sub> = 34.69 µg/ml	Sriwiriyajan et al. 2016
Analgesic	<i>In vivo</i> - Swiss albino mice	Fruit	Hexane Ethanol Compound: Piperine	Tail immersion method	Reaction time is the time taken by mice to withdraw the tail Maximum activity: Piperine: reaction time after 120 min at a dose of 5 mg/kg = 11.658 s Hexane: reaction time after 60min dose of 10 mg/kg = 8.284 s Ethanol: reaction time after 120 min dose of 15 mg/kg = 9.602 s	Tasleem et al. 2014
				Analgesy-meter	Sensitivity of animals to pain as determined by reaction time Maximum activity.  Piperine: reaction time after 60 min at a dose of 15 mg/kg = 9.400 s Hexane: reaction time after 60min dose of 5 mg/kg = 13.000 s Ethanol: reaction time after	
				Hot plate	Reaction time for paw licking or jumping Maximum activity: Piperine: reaction time after 30 min at a dose of 10 mg/kg = 12.870 s Hexane: reaction time after 120 min dose of 15 mg/kg = 2.738 s Ethanol: reaction time after 60 min dose of 5 ma/ka = 2.486 s	
				Acetic acid induced writhing test	Result expressed as number of writhes counted for 20 min commencing 5 min after injection of acetic acid. Maximum activity: Piperine (dose of 10 mg/kg) = 100.00% protection Hexane (dose of 5 and 10mg/kg) = 99.71% protection Ethanol (dose of 15mg/kg) = 100.00% protection	
Analgesic	<i>In vivo-</i> Male mice	Z	Compound: Piperine	Writhing test Tail-flick assav	At 70mg/kg, caused 89% inhibition of noci- ception induced by acetic acid	Bukhari et al. 2013
Anticonvulsant	In vivo- male Wistar Rats	Z	Ethyl alcohol n-Hexane	Pentylenetetrazol (PTZ) induced model Maximal electroshock seiz-	time from 3.7s (control) to 17.2s Piper nigrum suppressed onset and duration of seizures in both PTZ and MES models.	Belemkar et al. 2013
Anticonvulsant	Clinical-Adult epileptic patients	I	Compound: Piperine	ure (MES) Induced model –	Single oral dose of piperine (20 mg) increased the mean plasma concentration	Patnaik et al. 2012

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Bukhari et al. 2013	Yang et al. 2015	Hritcu et al. 2014	Hritcu et al. 2015	Correia et al. 2015			Pany, Abhisek, and Pratap2016	Kaleem, Sheema, Sarmad, and Bano2005	Onyesife, Ogugua, and Anaduaka2014	Gupta, Singh, and Jaqqi2014b	Vijayakumar and Nalini2006
of diphenyl hydantoin both in the absorption and elimination phases in both 150 and 200 mg dose-phenytoin patients groups.  50mg/kg piperine treatment was most effective than 70 mg/kg in preventing the animals from PTZ-induced seizures. The highest tested dose of piperine (70mg/kg) increased the latency of picrotoxininduced convulsions to 878.5 s compared to value of control group 358.4 s	Attenuated 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced deficits in motor coordination and cognitive functioning Also prevented MPTP-induced decrease in the number of tyrosine hydroxylase-positive cells in the substantia nigra. The compound also reduced the number of activated microglia, cytokine IL-1β expression, and oxidative stress following MPTP treatment.	Ameliorates amyloid beta(1–42)-induced spa-	tial memory impairment by attenuation of the oxidative stress in the rat hippocampus. Exhibited anxiolytic- and antidepressant- like effects	Piperine treatments reversed partially the decline in locomotor activity of the 6-OHDA (lesioned in the right striatum) group.	Piperine treatments fully inverted the motor deficit of the 6-OHDA group.	Piperine treatments inverted the increased number of apomorphine-induced contralateral rotations observed in the 6-OHDA group.	Administration of piperine increased the brain-plasma phenytoin ratio, GSH level, number of viable neurons and decreased lipid peroxidation and catalase activity.	Treatment of diabetic rats with <i>P. nigrum</i> extract for 4 weeks reduced the blood glucose level to 129 mg/100mL compared to diabetic rats (270 mg/100mL)	21 days treatment of 100, 200 and 300mg/kg body weight of <i>P. nigrum</i> extract reduced blood glucose level in alloxan induced diabetic rats.	$IC_{50}$ value $=35.64~\mu \mathrm{g/mL}$	Supplementing piperine to the high fat diet rats lowered the levels of plasma total cholesterol, LDL, VLDL tissue HMG CoA
Pentylenetetrazol (PTZ)- induced seizures Picrotoxin-induced seizures	Rotarod and Morris Water Maze (MWM) Test	Y-maze and radial arm-maze tasks	Elevated plus-maze test Forced swim- ming test	Open field test	Rotarod test	Apomorphine-induced rotations	Pilocarpine model		I	Goat lens aldose reductase inhibitorory activity	
Compound: Piperine	Compound: Piperine	Methanol	Methanol	Compound: Piperine			Piperine isolated from ethanol extract	Aquoeus	Ethanol	Methanol: Water mixture (3:1)	Compound: Piperine
≅ ≅	₹	Fruit	Fruit	Z			Seed	Seed	Leaf	Seed	I
<i>In vivo</i> - Male mice	<i>In vivo-</i> Male C57BL/6 mice	<i>In vivo</i> - Male Wistar rats	<i>In vivo</i> - Male Wistar rats	<i>In vivo</i> - Male Wistar rats			<i>In vivo</i> -Albino rats	<i>In vivo</i> - Male albino rats	In vivo- rats	In vitro	<i>In vivo</i> - Male Wistar rats
Anticonvulsant	Neuroprotective	Neuroprotective	Neuroprotective	Neuroprotective			Neuroprotective	Hypoglycemic	Hypoglycemic	Hypoglycemic	Hypolipidemic

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Table 3. Continued.	d.					
Activity	Model used	Plant Part	Extract	Assay	Findings	References
Hypolidemic	<i>In vivo-</i> Male Wistar rats	≅	Alcohol Compound: Piperine	ī	reductase and raised the levels of LPL and LCAT compared to rats that did not receive piperine.  Reduced levels of total cholesterol, free fatty acids, phospholipids and triglycerides in <i>P. nigrum</i> extracts (250mg/kg b.w and 500mg/kg b.w) as well as in the piperine (20mg/kg b.w) treated groups.  Supplementation with both <i>Piper nigrum</i> and piperine extracts increases the plasma HDL cholesterol and reduced the LDL and vLDL cholesterol.	Vijayakumar et al. 2002
Anti-inflammatory	<i>In vivo-</i> Swiss albino mice	Fruit	Hexane Ethanol Compound: Piperine	Carrageenan induced paw edema method	Maximum activity: Piperine: Reaction time after 120 min at a dose of 15 mg/kg) = 0.588 s Hexane: Reaction time after 60min dose of 10mg/kg) = 0.470 s Ethanol: Reaction time after 60min dose of 10mg/kg = 0.484 s	Tasleem et al. 2014
Anti-inflammatory	<i>In vivo</i> - Balb/C mice (20-25g)	Z	Essential oil	Carrageenan induced acute inflam-		Jeena et al. 2014
				matory model	500 mg/kg b.wt. essential oil produced 72 % inhibition at third hour compared to control	
				Dextran induced acute inflamma-		
				tory model	1000 mg/kg b.wt. essential oil reduced the paw thickness by 73.4 % at third hour compared to control	
				Formalin induced chronic inflamma-		
				tory model	500 mg/kg b.wt. essential oil produced 50 % % inhibitions of paw edema compared to control	



Part used	Extract type/ Isolated compounds	Microorganisms tested	Main findings	References
Fruit	Ethanolic	Gram-positive strains (B. subtilus, E. faecalis, S. xylosus, S. aureus and S. epidermidis), Gram-negative strains (E. coli, K. pneumoniae, S. enterica)	The MIC was <325 mg/mL against all strains tested. The most susceptible bacteria to the ethanol extract were S. aureus and B. subtilus with MIC value of 156.25 mg/mL	Zarai et al. 2013
Fruit	Compounds: 3,4-dihydrox- yphenyl ethanol gluco- side (A), 3,4-dihydroxy- 6-(N-ethylamino) ben- zamide (B)	S. aureus ATCC 6538B and B. cereus isolated from a food sample, S. typhimurium, E. coli DH5α	Both the compounds inhibited the growth of all of the four tested bacteria tested except that no inhibition was observed by compound A on S. typhimurium.  Compound A (MIC= 2.25 mmol/L) was more effective than compound B (MIC= 7.6 mmol/ L) but less effective than the positive control, 4-methylcatechol (MIC= 2 mmol/L).	Pradhan, Variyar, and Bandekar 1999
Fruit	Ethyl acetate Acetone Methanol	Bacteria: K. pneumonia 13883, B. megaterium NRS, P. aeroginosa ATCC 27859, S. aureus 6538 P, E. coli ATCC 8739, E. cloaca ATCC 13047, C. xerosis UC 9165, and S. faecalis DC 74) Fungi: Kluyveromyces marxianus, Rhodotorula rubra	The acetone extract did not show inhibition on any of the microorganisms tested, except for <i>C. xerosis</i> (ZOI = 7 mm). The methanol extract displayed no activity against <i>K. pneumoniae</i> , <i>P. aeruginosa</i> and <i>R. rubra</i> . The ethyl acetate extract exhibited no antimicrobial effect against <i>P. aeruginosa</i> , <i>S. faecalis</i> and <i>R. rubra</i> .	Keskin and Toroglu 201
Fruit	Ethanol	Isolated strains of <i>K. pneumoniae</i> from urine culture of hospitalized patients suffering from urinary tract infections	MIC= 0.62 mg/mL.	Sepehri et al. 2014
Leaf Fruit	Essential oil	Bacteria: <i>B. subtilis</i> (gram positive bacteria), <i>P. aeruginosa</i> (gram negative) Fungi: <i>C. albicans</i> , <i>Aspergillus niger</i> , <i>Penicillium spp</i> , <i>Saccharomyces cerevisiae</i> Dermatophyte: <i>Trichoderma spp</i>	Fresh berry oil was most effective against <i>Bacillus subtilis</i> (MIC= 1µg/mL) compared to other microorganisms. The dry berry oil and pepper leaf oil were most effective against <i>Saccharomyces cerevisiae</i> (MIC= 0.8µg/mL and 2.5/mL, respectively) than other microorganisms.	Sasidharan and Menon 2010
Fruit	Carbon tetrachloride Benzene Chloroform Ethyl acetate Acetone Ethanol Distilled water	Bacteria: Staphylococcus albus, Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli, Bacillus megaterium Fungus: Aspergillus niger	At a concentration of 40 μg/disc; Carbon tetrachloride extract was effective against all microorganisms (ZOI = 5–9mm) except for <i>S. typhi</i> . Benzene extract was most effective against <i>A. niger</i> (ZOI= 10–14 mm). Ethyl acetate, acetone and chloroform extracts were effective only against <i>S. albus</i> , <i>S. typhi</i> , <i>P. aeruginosa</i> and <i>A. niger</i> . (ZOI = 5–9 mm). The ethanolic extract of <i>P. nigrum</i> was most effective against <i>S. typhi</i> (ZOI = 10–14mm). The aqueous extract of <i>P. nigrum</i> was effective only against <i>E. coli</i> , <i>B. megaterium</i> , <i>S. albus</i> and <i>S. typhi</i> (MIC = 5–9mm).	Khan and Siddiqui 2007
Fruit	Petroleum ether	B. subtilis (MTCC 441), S. aureus (MTCC 96), K. aerogenes (MTCC 39), B. sphaericus (MTCC 511) and Chromobacterium violaceum (MTCC 2656)	At the highest concentration tested (100 $\mu$ g), <i>P. nigrum</i> was most effective against <i>B.</i> subtilis (ZOI = 12 mm) and <i>K. aerogenes</i> (ZOI = 13 mm).	Reddy et al. 2004
Fruit	Aqueous Methanol	Bacteria : Staphylococcus aureus, Bacillus subtilis, E. coli and Pseudomonas aeruginosa Fungi: Aspergillus niger and Candida albicans	All microorganisms were inhibited by both types of extracts at the highest concentration tested of 10 mg/mL (Aqueous: ZOI = 18–25 mm; Methanol: ZOI = -23 mm). <i>S. aureus</i> (ZOI = 25 mm) was inhibited to the highest extent by the aqueous extract whereas for the methanolic extract, both <i>S. aureus</i> and <i>E. coli</i> were the most inhibited (ZOI = 23 mm).	Trivedi et al. 2011
Fruit	Ethanol, Chloroform	Clinical bacterial isolates: Staphylococcus aureus, Salmonella typhi, Escherichia coli, Proteus mira- bilis and Pseudomonas aeruginosa	(201 = 23 mm).  At the highest concentration (4 mg/mL) of ethanol extract tested, <i>E. coli</i> was mostly inhibited (201 = 22mm). The chloroform extract was mostly effective against <i>E. coli</i> and <i>proteus</i> sp. (201 = 18mm)	Ganesh, Suresh, and Aranraj 2014
Fruit	Ethanol	Bacteria: <i>E. coli</i> and <i>S. aureus</i> Fungi: <i>A. niger</i> and <i>Mucor</i> species	At concentration of 500μg of extract, all microorganisms were inhibited (ZOI = 3.9–13.0 mm). The extract was most effective against S. aureus (ZOI =13 mm) but was less effective against the two fungal strains. (ZOI = 3.9–4.1 mm).	Reddy and Seetharam 2009

Table 4. Continued.

Part used	Extract type/ Isolated compounds	Microorganisms tested	Main findings	References
Fruit Seed	Cold water Hot water Methanol	Bacteria: Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa and Salmonella typhi	The extracts inhibited all the bacteria. Cold water extract had the maximum zone of inhibition against <i>E. coli</i> (ZOI = 23mm), hot water extract showed maximum zone of inhibition against <i>S. typhi</i> and <i>S. aureus</i> (ZOI = 22mm) and the methanolic extract showed maximum zone of inhibition against <i>E. coli</i> , <i>S. typhi</i> and <i>P. aeruginosa</i> (ZOI = 21mm), however the methanolic extract had no effect on <i>S. aureus</i> .	Khan et al. 2013
Fruit	Ethanol	Streptococcus mutans (MTCC 890, Enterococcus faecalis (MTCC 439), Lactobacillus acidophilus (MTCC 10307), Candida albicans (MTCC 854) and Candida tropicalis (MTCC 184).	The ethanolic extract inhibited all the microorganisms (ZOI $=$ 18–25 mm) except S. mutans.	Gauniyal, Vir, and Teotia 2014
Fruit	Acetone Dichloromethane	B. cereus (NCIM-2016), S. faecalis (NCIM-2016), E. coli (NCIM-2089), K. pneumonia (NCIM-2957), P. aer- ugonisa (NCIM-2200), S. typhi (NCIM- 2263)	The acetone extract was more active than the dichloromethane extract and <i>S. aureus</i> was inhibited to the highest extent (ZOI = 20 mm).	Karsha and Lakshmi 2010
Fruit	Methanol	Different clinical strains of Providencia stuartii, P. aeruginosa, K. pneumoniae, E. coli, Enterobacter aerogenes and Enterobacter cloacae	The methanolic extract of $P$ . nigrum showed some level of inhibition to all microorganisms but was most effective against $P$ . $aeruginosa\ PA01\ (MIC = 32\ \mu g/mL)$ .	Noumedem et al. 2013
Fruit	Methanol	P. aeruginosa, Klebsiella pneumoniae, E. coli, Proteus mirabilis and Staphylococcus aureus	The extract was most effective against Proteus mirabilis (ZOI= 5.00mm), followed by E. coli (ZOI = 4.90 mm) and Klebsiella pneumoniae (ZOI = 4.63 mm).	Ghaidaa, Aseel, and Haider 2016
Leaf	Ethanol, diethyl ether, chloroform and water	S. aureus, Bacillus sp., E. coli and Klebsiella sp.	The ethanol extract showed greatest activity against all the pathogens, the highest activity noted was against <i>Bacillus</i> sp.	Kavitha and Mani 2017
Leaf Stem	Aqueous	Citrobacter freundii and Erwinia cacticida	Silver nanoparticles from <i>P. nigrum</i> leaf were more effective against both <i>Citrobacter freundii</i> and <i>Erwinia cacticida</i> (ZOI = 8.962 and 9.052 respectively) than the silver nanoparticles synthesized from <i>P. nigrum</i> stem (ZOI = 8.894 and 9.012 respectively).	Paulkumar et al. 2014
Leaf	Aqueous Acetone Ethyl acetate	Bacteria: E. coli, B. subtitis, S. aureus, Enterobacter sp., Haemophilus sp. and Yersinia sp. Fungi: Cephalosporium sp., A. niger, P. notatum and C. albicans.	The ethyl acetate extract was most effective against the bacteria (ZOI = 14–20 mm) but it did not show any antifungal activity. The acetone extract showed moderate inhibition against C. albicans (ZOI = 14 mm), A. niger (ZOI = 10 mm), Cephalosporium sp. (ZOI = 14 mm), and P. notatum (ZOI = 18 mm). However, the aqueous extract did not show any significant antimicrobial property.	Shanmugapriya et al. 2012
Leaf	Aqueous Methanol Ethanol Petroleum ether	Bacteria: S. aureus (ATCC 25923), E. coli (ATCC 25922), S. typhimurium (ATCC 13311) and P. aeruginosa (ATCC 27853) Fungi: Aspergillus spp. (JUAS 27031) and C. albicans (ATCC 90028)	The methanol extract (ZOI = 11.67–20.00 mm) was found to be the most effective against all the bacteria compared to the ethanol (ZOI = 10.00–14.67 mm), petroleum ether (ZOI = 9.33–11.33 mm) and aqueous (ZOI = 8.00–9.33 mm) extracts. <i>E. coli</i> was the microorganism that were most inhibited by all the <i>P. nigrum</i> extracts. Among the two fungi tested, <i>Aspergillus spp.</i> (ZOI = 11.33–19.67 mm) was inhibited higher than <i>C. albicans</i> (ZOI = 8.33–12.67 mm).	Akthar, Birhanu, and Demisse 2014
Leaf	Aqueous Ethanol	S. mutans, Phorphyromonas gingivalis	Only the aqueous extract was effective against <i>S. mutans</i> (MIC = 125 µg/mL). The ethanolic extract did not show any inhibition against both bacteria.	Rosas-Pinon et al. 2012
Leaf	Aqueous	E. coli and B. subtilis	The aqueous extract of <i>P. nigrum</i> was only effective against <i>B. subtilis</i> (ZOI = 8 mm).	Jain, Bansal, and Bhasin 2010
Seed	Aqueous Ethanol Petroleum ether	S. aureus (NCTC 25953), E. coli (NCTC 25922), S. typhi (NCTC 25936), P. aeruginosa (NCTC 27853)	Only <i>S. aureus</i> was inhibited by the petroleum ether extract (At 100% concentration: ZOI = 15mm). The ethanolic extract (ZOI =	Gadir, Mohammed, and Bakhiet 2007

Table 4. Continued.

Part used	Extract type/ Isolated compounds	Microorganisms tested	Main findings	References
	·	-	14–18mm) inhibited all bacteria except <i>S. aureus</i> . The aqueous extract inhibited only <i>S. aureus</i> and <i>S. typhi</i>	
Seed	n-Hexane Acetone Ethanol Aqueous	S. aureus, B. subtilis, E. coli, and P. aeruginosa	At a concentration of 1000 μg/disc; There was no bacterial inhibition with the n-Hexane solvent. <i>S. aureus</i> and <i>B. subtilis</i> were the only bacteria inhibited by the acetone (ZOI = 9 mm) and ethanol extract (ZOI = 10–11 mm). The aqueous extract was the most effective as it inhibited <i>S. aureus</i> (ZOI = 10 mm), <i>B. subtilis</i> (ZOI= 9mm) and <i>P. aeruginosa</i> (ZOI = 13mm).	Penecilla and Magno201
Seed	Hexane Dichloromethane Ethanol Aqueous	S. aureus (MTCC 3160), E. coli (MTCC 119), S. typhi (MTCC 531) and B. subtilis (MTCC 121)	All the extracts tested had some level of inhibition. The dichloromethane extract had the highest activity against all the bacteria ( $ZOI = 10-19$ mm, $MIC = 2-10$ mg/mL). The aqueous extract had the lowest activity against all the bacteria ( $ZOI = 7-9$ mm; $MIC: >40$ mg/mL).	Gupta et al. 2014a
Seed	Hot water Cold water Pepper soup	E. coli, S. aureus, and C. albican	The hot water extract had the highest mean ZOI on all the bacteria tested (mean ZOI = 13.775mm). The extracts were most effective against <i>E. coli</i> (mean ZOI = 13.548 mm).	Kalunta2017
Seed	Ethanol	Bacteria: B. subtilis (ATCC 6633), S. aureus (ATCC 25923), S. epidermidis (ATCC 12228), E. coli (ATCC 25922), P. aeruginosa (ATCC 10145) Fungi: Candida albicans (ATTC 60192), and A. niger	The extract was most effective against <i>P. aeruginosa</i> (MIC = 5 mg/mL). Among the fungi, <i>A. niger</i> was mostly inhibited (ZOI = 15 mm).	Erturk2006
Seed	Essential oil	A. niger and G. candidum	The extract was more effective against <i>G.</i> candidum at 20 ppm and 30 ppm of concentrations tested.	Verma, Chaurasia, and Kumar2011
NI	Aqueous Methanolic Ethanolic	B. subtilis, B. megaterium, B. sphaericus, B. polymyxa, S. aureus (Grampositive), and E. coli (Gram-negative) and eleven molds, A. luchuensis, A. flavus, P. oxalicum, R. stolonifer, Scopulariopsis sp. and Mucor sp.) isolated from bakery products and pickles.	The aqueous extracts showed antibacterial activities against all bacterial strains (ZOI = 11—30 mm) except against <i>B. subtilis</i> . The methanolic extract, (ZOI = 12–28 mm) was more effective than the ethanolic extract, (ZOI = 15—22 mm). No antifungal activities were observed with any of the extracts.	Pundir and Jain2010
NI	Essent <b>® God</b> m-positive and 16		Of all the bacteria tested, only 3 were not inhibited by the volatile oil. <i>Aeromonas hydrophila</i> (NCTC 8049) was mostly inhibited (over 90.0 mm).	Dorman and Deans2000
NI	Ethanol	K. pneumoniae, S. aureus, M. morgani, C. albicans, E. coli and P. vulgari	At the highest concentration tested (2000 ppm), the ethanolic extract inhibited all the microorganisms (ZOI = 6–16mm), except <i>M. morgani</i> . The extract was most effective against <i>E.coli</i> (ZOI = 16mm).	Joe, Jayachitra, and Vijayapriya2009
NI	Alcohol	Bacteria: Pseudomonas lundensis and Bacillus cereus Fungi: Aspergillus niger and Aspergillus flavus	At 100% of the extract, all microorganisms were inhibited (ZOI = 10–12mm). The extract was most effective against <i>B. cereus</i> (ZOI = 12 mm). However, at lower concentrations tested (25, 50, 75%), not all microorganisms were inhibited.	Hema, Kumaravel, and Elanchezhiyan2009
NI	Aqueous	Clinical isolates of S. aureus, Salmonella sp., Bacillus subtilis and E. coli.	The aqueous extract was found to be most effective against <i>B. subtilis</i>	Ghori and Ahmad2009
NI	Methanol	S. aureus P. aeruginosa, E. coli, S. tuphiumirium	At 50 mg/mL concentration, the methanolic extract inhibited all the bacteria. (ZOI = 9.75–12.25 mm).	ShivaRani and Neeti2013
NI	Aqueous Ethanol Methanol	S. aureus, B. subtilis, B. cereus, E.coli, S. typhi, P. aeruginosa	The aqueous extract inhibited only the gram-positive bacteria ( $ZOI = 12-17 \text{ mm}$ ). The methanolic extract inhibited all bacteria ( $ZOI = 11-18 \text{ mm}$ ) except <i>B. subtilis</i> . The	Shete and Chitanand2014

Table 4. Continued.

Part used	Extract type/ Isolated compounds	Microorganisms tested	Main findings	References
			ethanolic extract was the most effective (ZOI = 16–22 mm).	
NI	Aqueous Ethanol Chloroform Methanol	E. coli (MTCC-40), P. aeruginosa (MTCC-424), Salmonella sp. (MTCC- 3215), Shigella flexneri (MTCC1457), S. aureus (MTCC-3160)	Methanol extract was ineffective against all the bacteria. The aqueous (ZOI= 1-3mm) and ethanolic extract (ZOI = 3-5 mm) showed moderate inhibition on all the bacteria. The chloroform extract also showed inhibitory effects on all the bacteria (ZOI = 1-6 mm) but was most effective against <i>S. flexneri</i> (ZOI = 6 mm).	Debnath et al. 2014
NI	Aqueous Methanol Ethanol Acetone Petroleum ether	E. coli, K. pneumoniae, Proteus sp., P. aeruginosa, and B. subtilus	All extracts inhibited all the bacteria. At 50% v/v, the methanol extract exhibited significant inhibition of all the bacteria (ZOI = 10–14 mm). Petroleum ether extract showed the lowest activity on all the microorganisms (ZOI = 4–6 mm)	Renu, Ekta, and Neha201
NI	Essential oil	Propionibacterium acnes (DMST No. 14916, 14917, 14918, 21823, 21824)	P. nigrum oil was ineffective against all of the bacterial strains.	Luangnarumitchai, Lamlertthon, and Tiyaboonchai2007

<sup>\*\*</sup>Due to the high number of bacteria tested (n = 25), the list of bacteria was not added to the table.

316.27 µg/mL). The ABTS scavenging effect of the essential oil (IC<sub>50</sub>= 223.8 mg/mL) was also determined by (Zhang and Xu 2015).

Phenolic compounds from P. nigrum including 3,4-dihydroxyphenyl ethanol glucoside, 3,4-dihydroxy-6-(N-ethylamino) benzamide, and phenolic acid glycosides were found to scavenge DPPH radicals, with EC<sub>50</sub> values of 0.076, 0.27, and 0.12 mg/mL, respectively (Chatterjee et al. 2007). Another P. nigrum compound, N-trans-feruloyltyramine, also showed potent DPPH inhibition (EC<sub>50</sub> =  $11.82 \,\mu\text{g/mL}$ ) (Tu et al. 2016). Isolated compounds such as piperine and piperic acid also showed higher DPPH and antioxidant activity in the phosphomolybdenum assay compared to the ethanolic extract of the berries. Piperine was more potent DPPH scavenger compared to piperic acid (10.28 and 29.5% inhibition, respectively, at 50 µg/mL) while piperic acid displayed higher molybdenum (VI) reducing activity (64.1 and 58.8 μmol/mL α-tocopherol equivalents at 100 μg/mL, respectively) (Zarai et al. 2013).

*In vivo* experiments also revealed that *P. nigrum* extracts improved the level of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione-S- transferase (GST), and the reduced glutathione (GSH) (Vijayakumar, Surya, and Nalini 2004). Also, concurrent piperine (40 mg/kg body weight in 1% carboxymethyl cellulose, p.o) supplementation along with highfat diet and antithyroid drug administration reduced lipid peroxidation and improved the antioxidant status compared to those rats which did not receive piperine treatment (Vijayakumar and Nalini 2006).

# **Anticancer**

The increasing resistance and associated adverse effects of chemotherapeutic drugs, and the recurrence of cancer have increased the interest in the scientific community to explore for new agents from medicinal plants. Researchers have proved anticancer property of P. nigrum and its bioactive compounds against different cancer cell lines. For instance,

the chloroform and petroleum ether extract of the root showed the cytotoxic effect against human myeloid leukemia HL-60 cell (IC<sub>50</sub> = 9.8 and 11.2  $\mu$ g/mL, respectively after 72 h of exposure) (Ee et al. 2009). The methanol extract of the fruit was more effective than the dichloromethane extract against the breast cancer MCF-7, and MDA-MB-231 cell lines while the latter showed higher cytotoxicity against MDA-MB-468 cell (Sriwiriyajan et al. 2014). The ethanolic extract of the fruit was also found to exhibit the anticancer effect on the three colorectal cancer cell lines (HT-29, HCT-116, and HCT-15) with IC<sub>50</sub> values of 7.4, 3.4, and 1.9  $\mu$ g/ mL, respectively (Prashant et al. 2017).

Two active compounds isolated from the fruit, (-)-kusunokinin and piperlonguminine, displayed cytotoxic effect against breast and colorectal cancer cells. (-)-kusunokinin showed greater cytotoxicity to MCF-7, MDA-MB-468, and SW-620 (IC<sub>50</sub> = 1.18, 1.62, and 2.60  $\mu$ g/mL, respectively), while piperlonguminine was more efficient on MDA-MB-231 (IC<sub>50</sub> =  $71.54 \,\mu\text{g/mL}$ ). Both compounds displayed lower cytotoxicity against normal breast cell lines with IC50 values higher than 11 µg/mL. Besides, the compounds induced cell apoptosis and drove cells towards the G2/M phase. Also, both compounds decreased topoisomerase II and Bcl-2. The increase in the level of p53 further increased p21, bax, cytochrome c, caspase-8, -7 and -3 activities (Sriwiriyajan et al. 2017).

Another compound from the root, pellitorine, was found to be cytotoxic against MCF-7 (IC<sub>50</sub> =  $1.8 \,\mu g/mL$ ) and HeLa (IC<sub>50</sub> =  $13 \,\mu\text{g/mL}$ ) (Ee et al. 2009). The *P. nigrum* compound mostly studied for its anticancer properties is piperine which was found as a potent cytotoxic agent against HER2-overexpressing breast cancer cells (SKBR3 and MCF-7 cell). Piperine strongly inhibited proliferation and caused apoptosis through activation of caspase-3 and PARP cleavage. Moreover, piperine inhibited the expression of HER2 gene at the transcriptional level. Piperine also blocked ERK1/2 signaling and reduced the expression of SREBP-1 and FAS. In addition, piperine actively suppressed EGFinduced MMP-9 expression via the inhibition of AP-1 and NF-jB activation by interfering with ERK1/2, p38 MAPK, and Akt signaling pathways, thereby causing a reduction in migration. Also, piperine pretreatment was found to enhance sensitization to paclitaxel killing in HER2-overexpressing breast cancer cells (Do et al. 2013).

Piperine also showed anticancer property against prostate cancer cell (LNCaP, PC-3 and DU145) (Ouyang et al. 2013). Treatment with piperine resulted in a dose-dependent inhibition of the proliferation of these cell lines. Piperine induced cycle arrest at G0/G1 and downregulated cyclin D1 and cyclin A. The compound also dose-dependently increases the level of p21Cip1 and p27Kip1 in both LNCaP and DU145 but not in PC-3 cells, which was in conformity with the more robust cell cycle arrest observed in the former two cell lines than the latter one. In addition, piperine induced autophagy as proved by an increase in the level of LC3B-II and LC3B puncta formation in LNCaP and PC-3 cells.

Piperine also re-sensitised P-glycoprotein, multidrug resistance protein 1 (MRP1) and breast cancer resistance protein (BCRP) dependent multidrug resistant cancer cells (Li et al. 2011). In vivo administration of piperine caused a 95.2% reduction in tumor nodule formation, serum sialic acid level and serum gamma-glutamyl transpeptidase activity in mice. The compound also suppressed benzo(a)pyrene (B(a)p) induced lung cancer in mice by decreasing the levels of total protein and protein-bound carbohydrate components (hexose, hexosamine, and sialic acid) (Selvendiran, Prince Vijeya Singh, and Sakthisekaran 2006).

# **Anti-inflammatory**

Tasleem et al. (2014) evaluated the anti-inflammatory effect of P. nigrum and its active compound piperine based on carrageenan-induced paw edema using plethysmometer. Piperine exhibited inhibition of edema at all doses of 5, 10, and 15 mg/kg. The compound showed maximum activity at a dose of 15 mg/kg after 120 min (Reaction time = 0.588 s) but still less than the standard drug diclofenac sodium (Reaction time = 1.330 s after 60 min). In addition, Jeena et al. (2014) observed that, using a carrageenan-induced acute inflammation model, administration of 500 mg/kg b.wt. P. nigrum essential oil significantly reduced paw edema by 72% in mice in the third hour when compared to the control group. On the other hand, treatment with 100 mg/kg oil produced 66.1% inhibition in the third hour. Moreover, using a dextran-induced acute inflammation model, the oil, at 100, 500, and 1000 mg/kg bw, dose-dependently reduced the paw thickness by 33.3, 53.3, and 73.4%, respectively, at the third hour when compared to the control group. The essential oil also showed a promising result compared to the standard drug Diclofenac (49.3% inhibition at 10 mg/kg). In the case of chronic inflammation induced by formalin, the P. nigrum essential oil caused a 50% inhibition of paw edema at 500 mg/kg while the inhibition exhibited by the standard drug diclofenac at 10 mg/kg was 57.5%.

# **Analgesic and anticonvulsant**

The interest in the exploration for novel and safe pain-alleviating natural agents has stimulated scientists to study P. nigrum as a therapeutic pain agent. Tasleem et al. (2014) determined the analgesic activity of hexane and ethanolic extracts of P. nigrum and its compound piperine using the tail immersion, analgesy-meter, hot-plate, and acetic acid induced writhing test. In the tail immersion method, piperine showed the maximum analgesic effect after 120 min at a dose of 5 mg/kg (reaction time by mice to withdraw the tail = 11.658 s) while in the analgesy-meter test, the ethanol extract was most effective after 60 min dose of 10 mg/kg (reaction time = 20.900 s). The highest reaction time for paw licking or jumping in the hot plate method was exhibited by piperine (12.870 s after 30 min at a dose of 10 mg/ kg). In the writhing test, piperine (dose of 10 mg/kg) and the ethanol extract (dose of 15 mg/kg) completely stopped the number of writhes in mice induced by acetic acid.

Additionally, the anticonvulsant effect of P. nigrum was also studied. Belemkar, Kumar, and Pata (2013) observed that the ethyl alcohol and hexane extract of P. nigrum suppressed the onset and duration of seizures in Wistar rats using both pentylenetetrazol (PTZ) induced model and maximal electroshock seizure (MES) induced model. In addition, Bukhari et al. (2013) found that 50 mg/kg piperine treatment was most effective than 70 mg/kg in preventing the animals from PTZ-induced seizures. The highest tested dose of piperine (70 mg/kg) increased the latency of picrotoxininduced convulsions to 878.5 s compared to the value of control group 358.4 s.

#### Hypoglycemic and hypolipidemic

Treatment of diabetic rats with P. nigrum aqueous seed extract for 4 weeks reduced the blood glucose level to 129 mg/100 mL compared to diabetic rats (270 mg/100 mL) (Kaleem, Sheema, Sarmad, and Bano 2005). 100, 200, and 300 mg/kg body weight of the leaf methanolic extract of P. nigrum reduced blood glucose level in alloxan induced diabetic rats after 21 days of treatment (Onyesife, Ogugua, and Anaduaka 2014). Aldose reductase is primarily involved in the development of long-term diabetic complications due to increased polyol pathway activity, therefore, its pharmacological inhibition has been recognized as an important strategy in the prevention and attenuation of associated complications particularly retinopathy, neuropathy, and nephropathy. Indeed, the study by Gupta, Singh, and Jaggi 2014b observed that the hydromethanolic extract of the seed inhibited goat lens aldose reductase, with an IC50 value of  $35.64 \mu g/mL$ .

Supplementing piperine to the high fat diet rats lowered the levels of plasma total cholesterol, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), HMG CoA reductase and raised the level of lipoprotein lipase (LPL) and lecithin-cholesterol acyltransferase (LCAT) compared to rats which did not receive piperine (Vijayakumar and Nalini 2006). Vijayakumar et al. (2002) also found reduced level of total cholesterol, free fatty acids, phospholipids, and



triglycerides in P. nigrum extracts (250 mg/kg b.w and 500 mg/kg b.w) as well as in the piperine (20 mg/kg b.w) treated groups. Supplementation with both P. nigrum and piperine extracts increased the plasma HDL cholesterol and reduced the LDL and VLDL cholesterol.

# Neuroprotective

A study by Hritcu et al. (2015) found that the methanolic extract of P. nigrum fruit exhibited anxiolytic- and antidepressant-like effects in male Wistar rats. The extract ameliorated amyloid beta (1-42)-induced spatial memory impairment by attenuation of the oxidative stress in the rat hippocampus (Hritcu et al. 2014). The compound piperine was found to attenuate 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced deficits in motor coordination and cognitive functioning (Yang et al. 2015). In addition, Correia et al. (2015) observed that piperine reversed partially the decline in locomotor activity, fully inverted the motor deficit, and inverted the increased number of apomorphineinduced contralateral rotations observed in the 6-OHDA (lesioned in the right striatum) group.

# **Toxicity**

Natural plant products have always been considered "safe" for centuries. However, this statement is not always right, especially when considering the dose of the plant product being administered. In this context, P. nigrum and/or its active compounds at a specific dose has also been documented to be potentially toxic by both in vivo and in vitro studies.

Tasleem et al. (2014) found that intraperitoneal administration of 25, 50 and 75 mg/kg of piperine in Swiss albino mice caused irritation and also observed drowsy after 30 min, while paralytic effect on hind limbs were noticed after more than 3hours with no intake of water and feed. More importantly, all six animals receiving 75 mg/kg of piperine died after 24 h, while animals treated with 25 and 50 mg/kg were found dead after 48 h.

The acute toxicity of piperine was also assessed on mice, rats, and hamsters. Single administration i.v., i.p., s.c., i.g. and i.m. to adult male mice displayed  $LD_{50}$  values of 15.1, 43, 200, 330 and 400 mg/kg body weight, respectively. Interestingly, in adult female mice. the i.p. the LD<sub>50</sub> value was increased to 60 mg/kg body weight while in weanling male mice, it was increased to 132 mg/kg body wt. In adult female rats, the i.p.  $LD_{50}$  value was 33.5 mg/kg body weight which was lower compared to the i.g. LD<sub>50</sub> value (514 mg/kg body wt). In addition, most animals receiving a lethal dose of piperine died within 3-17 min due to respiratory paralysis. In the subacute toxicity studies, the rats died within 1-3 days (Piyachaturawat, Glinsukon, and Toskulkao 1983).

Chunlaratthanaphorn et al. (2007) found that a single oral administration of the aqueous extract of the P. nigrum dried fruits (5,000 mg/kg body weight) to male and female Sprague-Dawley rats did not produce signs of toxicity, behavioral changes, mortality, changes on gross appearance or histopathological changes of internal organs. In addition, the subchronic toxicity was assessed by oral feeding daily at the doses of 300, 600 and 1,200 mg/kg body weight continuously for 90 days. No abnormalities were observed in the test groups as compared to the controls.

# Conclusion and future perspectives

From the above review, a disproportion in the amount of reported folk medicinal knowledge on P. nigrum was observed in some countries. Since it is a popular spice globally used, further studies should emphasize on conducting surveys on the traditional uses of P. nigrum in other regions as well, together with a well-reported method of preparation and dosage taken. Moreover, it was observed that most pharmacological studies were conducted in vitro (n = 60)while only 21 in vivo and 1 clinical trial was performed. Hence, further in vivo experiments together with a pharmacokinetic and pharmacokinetic approach would be beneficial. Nonetheless, in vitro studies are still required to screen for most potent solvent extracts and fractions, and to understand the mechanism of action such as the enzyme inhibitory pathway through molecular docking. For instance, the observed in vivo neuroprotective effects of P. nigrum could be further studied in vitro with regards to its potential acetylcholinesterase and butyrylcholinesterase inhibition, two key enzymes involved in Alzheimer's and Parkinson disorders. Similarly, research on the inhibitory effect of P. nigrum against α-amylase, α-glucosidase, and lipase enzymes could provide information on the mechanism of the in vivo hypoglycemic and hypolipidemic action previously observed. Future studies may also explore the interactions of the potent compound piperine with other compounds present in P. nigrum, and also in combination with current conventional drugs, in order to observe any synergistic or additive effect, which may ultimately lead to a reduced therapeutic dose with less associated toxicity. To conclude, P. nigrum is not only a widely used spice but is also an important medicinal plant which may be considered as potential nutraceutical and pharmaceutical agents.

# List of abbreviations

AOA antioxidant activity W-body weight conjugated dienes CD COX cyclooxygenase

DPPH- 1 1-Diphenyl-2-picryl-hydrazyl

FC-Folic-Ciocalteu; FOS fructo-oligosaccharide

Fast protein liquid chromatography **FPLC FRAP** ferric reducing antioxidant power

FW Fresh Weight; g-gram GAE Gallic acid Equivalent HDL high-density lipoproteins

HP hydroperoxide

**HPLC** High-performance liquid chromatography

ZOI Zone of Inhibition

Kg Kilogram

LDL low-density lipoproteins vLDL very low-density lipoproteins



LOX lipoxygenase malondialdehyde MDH

milligram mg

MIC Minimum Inhibition Concentration

mililitre mL

National Onion Association NOA

oС Degrees celcius

Peripheral blood mononuclear cells **PBMCs** 

**SMCS** S-methyl cysteine sulfoxide SOD superoxide dismutase

Trolox equivalent antioxidant capacity **TEAC** 

TLC Thin layer chromatography

microgram μg microliter μl

LD50 lethal dose to kill 50% population

intraperitoneal i.p ; i.v intravenous subcutaneous s.cintragastric ; i.g intramuscular i.m

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