Review Article

www.ijrap.net

VISHA BILWADI GUTIKA: A REVIEW

G. Sunitha *[1], Gazala Hussain [2]
[1]PG Scholar, Department of Agada Tantra, Sri Dharmasthala Manjunatheswara College of Ayurveda & Hospital, Hassan, Karnataka, India
[2]Associate Professor, Department of Agada Tantra, Sri Dharmasthala Manjunatheswara College of Ayurveda & Hospital, Hassan, Karnataka, India

Received on: 20/03/17 Accepted on: 24/04/17

***Corresponding author**
E-mail: sunithagopakumar1@gmail.com

DOI: 10.7897/2277-4343.08281

ABSTRACT

Visha bilwadi gutika is explained in Kriya kaumadi, a Malayalam book by Kuttikrishna menon. It contains all ingredients similar to Bilvadi gutika, with addition of neelini (*Indigofera tinctoria*), eshvari (*Aristalochia indica*) and pada *(Cyclea peltata*). This formulation is mainly indicated in darvikara visha (cobra bite). Most of drugs of Visha bilwadi agada has ushna veerya, vataghna and kaphghna property. By these properties the drug visha bilwadi agada may give relief in various signs and symptoms produced due to visha like swelling, itching and urticarial actions. Most of the drug having anti-inflammatory, analgesic, cardio protective and neuro protective activity. These actions are needed in case of envenomation. The hrudya and vishagna properties of the drugs reduce the signs and symptoms of venomous bite. Various studies have proved that some drugs have ante venom activity also. The main objective of this review article is to discuss the different pharmacological properties of its contents with respect to cobra bite.

Key Words: Visha bilwadi gutika, darvikara visha, neelini, eshvari, pada

INTRODUCTION

Snake bite is said to be a major health hazard worldwide. The number of accidents globally have reached a million and more than 20,000 deaths annually. In India alone more than 200,000 cases are reported and an estimated 35,000 to 50,000 people die each year[1]. Cobra is responsible for large number of snake bite causalities reaching 65% of envenomation in the country. Most common symptom in cobra bite are pain and numbness of an ascending nature. The spread of venom is very fast in cobra bite and if a lethal quantity of venom (12g) is injected the patient may die within 30-40 minute[2]. Anti-venom is the only therapeutic agent available throughout the world. In the rural areas snake bite victims depend on traditional medicine only, due to lack of availability of antivenom. A formulation mentioned in kriya kaumadi is visha bilwadi gutika indicated in darvikara bite (cobra). The ingredients are similar to vilwadi gutika. The additional drugs mentioned are neelini (*Indigofera tinctoria*), ishvari (*Aristalochia indica)* and pata *(Cyclea peltata)*[3]. All the drugs in this yoga are krimighna and vishaghna. And their pharmacological actions revealed as antimicrobial, antiviral, anti-inflammatory, analgesic, cardio protective, antiseptic, antifungal, antidiarrheal and anti protozoal[4].

INGREDIENTS OF VISHA BILWADI GUTIKA

BILWA

Bilva (*Aegle marmelos*) is extensively described and used in the Vedic literature. Bilva is considered as best sangrahika and deepaniya drug being vata kaphahara**.** Stem is good for the heart, effective in rheumatoid arthritis and improves secretion of digestive enzymes. Unripe fruits balance Kapha and Vata doshas. Ripe fruits are difficult to digest and aggravate all three doshas[5]. The study shows that bilva is having anti- oxidant property. The herbal drugs those show anti-oxidant activity are safe for the use in the treatment of various disease because they do not produce toxic effect in the human body[6]. The role of oxidative stress in genesis of neurodegenerative diseases has been widely studied. The high oxygen consumption rate coupled with low antioxidant potential of the brain is the main triggering factor for the enhanced release of free radical. The study shows that that *Aegle marmelos* may be effective in the therapy of various neurodegenerative diseases, which may be due to effective free radical scavenging property of the plant [7].

Analgesic activity
Study shows that the methanol extract of leaves of *Aegle marmelos* at a dose level of 200 and 300 mg/kg and observed significant analgesic activity on acetic acid induced writhing and tail flick test in mice[8]

Anti-inflammatory and Cardio protective effects
The study shows that aqueous extract of *Aegle marmelos* with the help of rat paw oedema model and assured that *A. marmelos* have anti-inflammatory activity. The various extracts of the leaves of Bael were evaluated for anti-inflammatory activity. The cardio protective activity is due to the presence of aurapten as potent compound. The leaf extract of Bael has preventing effects in isoprenaline-induced myocardial infarction in rats. Further studies concluded that Bael can be used as cardiac depressant[9].

TULASI

Tulasi has been used for thousands of years in ayurveda for its diverse healing properties. It is regarded in Ayurveda as a kind of "elixir of life" and believed to promote longevity[10].

Anti-oxidant property
The antioxidant property of the O. Sanctum plant was stained by dot blot assay method. From this result, methanolic extracts showed maximum antioxidant potential than the other extracts.

This dot blot assay confirmed that these plants have the potential antioxidant property[11].

Analgesic activity
The 'rat tail method' was used to find out the analgesic effect. Tulasi showed an increase of 20.34 percent from mild dose, 43.80 per cent from moderate dose and of 51.47 per cent from maximum dose. The effect would remain up to 3 hours with all the three doses. The higher concentration of dose showed better efficiency. The results depict that Tulasi had a long-lasting analgesic effect so can be effective in chronic pains[12].

Anti-inflammatory activity
Ocimum santum alone and in combination with indomethacin was studied using Carrageenan-induced rat paw edema. Aqueous extract of O. sanctum (200mg/kg or 400mg/kg) was administered alone and in combination with indomethacin (25mg/kg) to separate group of rats and paw volume was measured by plethysmometer and compared with control group. All the test groups showed significant ($P<0.05$) anti-inflammatory effect in Carrageenan-induced rat paw edema. The reduction of edema by O. sanctum was better than that of the standard anti-inflammatory drug[13].

Neuro protective activity
Different extracts of stem, leaf and stem callus was tested for anticonvulsant activity by maximal electroshock model using phenytonin standard. It was observed that ethanol and chloroform extract of stem, leaf, stem callus were effective in preventing tonic convulsion induced by trans corneal electroshock[14].

Cardio protective and Wound healing property.
Prolong administration of fresh *Ocimum sanctum* leaves augments cardiac endogenous anti-oxidants and prevents isoproterenol induced myocardial necrosis in rats. It was observed that *Ocimum sanctum* at a dose 50 mg/kg are found to demonstrate maximum cardio-protective effect. Several studies show that healing property of *Ocimum sanctum.* Wound healing property of cold aqueous extract of *Ocimum sanctum* leaves along with its effect on tumor necrosis factor alpha was assessed using excision model of wound repair in albino rats. After application of *Ocimum sanctum* extract rate of epithelization with an increase in wound contraction was observed[15].

KARANJA

Karanja (*Pongamia pinnatta*) is mentioned among the kandughna varga (itching) by Charaka. It is mentioned in Rigveda and atharva veda. Karanja sticks are fore bidden for rituals but described as the best among tooth sticks. It is distributed throughout India. It is indicated in arshas (piles), grahani (IBS), unmade (insanity) etc. Chemical constituents are karanjin, pongapin, kanjone, pongol, gamatin, glabrin, 3-methoxy pongapin[16].

Analgesic and Anti-inflammatory activity
The ethanol extract of Karanja was investigated for anti-inflammatory and analgesic activity at the doses (p.o.) of 100, 200, and 400 mg/kg body weight. For evaluation of inflammation carrageenan, histamine- and serotonin induced paw edema served as acute models and cotton pellet–induced granuloma served as a chronic model in rats. The data obtained in this study demonstrated that extract of karanja might have analgesic and anti-inflammatory activities [17].

Antioxidant and Antimicrobial properties
A study conducted on "Antioxidant, Antimicrobial Properties and Phenolics of different Solvent Extracts from Bark, Leaves and Seeds of *Pongamia pinnata*" shows that the tested parts of *Pongamia pinnata*, in particular the bark, have better potential for the isolation of antioxidant and antimicrobial agents for pharmaceutical uses than the leaves and seeds[18].

TAGARA

(*Valeriana wallichi*) grows at 1000 ft in Himalayan region. Its useful part is root and is indicated in apasmara (epilepsy), anidra (sleeplessness), siroruk (head ache). Main chemical compositions are hydroxy valeranone, acctoxyvaleranone, linarin, isovalerate, didrovaltratum, valerosidatum, valtrate, acevaltrate[19].

Analgesic activity
A study has shown that both weak central and strong peripheral antinociceptive effect of *Valeriana wallichi*. The data suggested that essential oil exerted peripheral antinociceptive effect via inhibition of prostaglandin synthesis and central analgesic action via opioidergic pathway[20].

Anti-oxidant activity
The methanolic extracts of *Valeriana wallichi* was used in study and also screened for the presence of phyto-chemicals viz. alkaloids, flavonoids, tannins, saponins, glycosides, etc. and their effect on 2,2-Diphenyl-1-picryl-hydraxyl radical (DPPH) which was used to determine the free radical scavenging activity. The occurrence of phytochemical compounds in huge quantity is realistically proportional to the antioxidant activity[21].

Anti-inflammatory activity
Valeriana wallichi was found to be having anti-inflammatory property at dose of 40mg/kg and the anti-inflammatory property of *Valeriana wallichi* is increased with increasing dose[22].

DEVADARU

It is distributed in northwest Himalayan region. Major chemical constituents are p-methyl acetophenone, atlantone, sesquiterpenes, deodarin, toxifolin. Its useful part is kanda sara and is indicated in kasa (cough), swasa (asthma), krimi (worms), kandu(itching), kushta (skin disease), sopha (swelling).[23]

Neuroleptic, Anti- oxidant, Anti convulsant properties[24]
Traditionally the heartwood of *Cedrus deodara* plant was used to enhance cerebral function, balance the mind, body connection, nervous system and strengthen the brain. It was reported to possess CNS depressant and neuroleptic activity. C. deodara was also reported to have good antioxidant property. Two processes were involved to identify the antioxidant components of *Cedrus deodara.* Fractionation and purification was done of dried heartwood powder of C. deodara, first defatted with petroleum ether and then extracted with chloroform. The heart wood extracts of *Cedrus deodara* (ALCD) was studied for anxiolytic and anticonvulsant activity by three experimental models namely Elevated plus maze test, Light dark model, locomotor activity by actophotometer and anticonvulsant activity was studied by using Pentylene tetrazole induced convulsion. It shows good result also.

Wound healing property:
The oil has been reported to possess anti-inflammatory and anti-microbial activities. The plant has also shown wound healing properties and is particularly useful in infective wounds[25].

HARITHAKI

Harithaki (*Terminalia chebula*) is one of the important herbs used in folklore medicine, house hold and traditional medicine. Its fruit rind is used in medicine and one of the ingredients in Triphala.

Chemical constituents are antraquinone glycoside, chebulinic acid, tannic acid. It is indicated in sotha (swelling), prameha (diabetes), kushta (skin disease), vrana (ulcer)[26].

Cardio protective activity
Protective effect of *Terminalia chebula* against lysosomal enzyme alterations in isoproterenol induced cardiac damage in rats was studied. Pretreatment with an ethanol extract of *Terminalia chebula* was found to retain near normal activities of lysosomal enzymes in rats given *Terminalia chebula.* In vitro study with various extracts of the fruit rind showed cardio tonic activity in experiments with normal and hypodynamic isolated frog hearts. It increased the force of contraction and cardiac output without altering the heart rate[27].

Anti-oxidant and Neuro protective activity
The scavenging capacity of *Terminalia chebula* for the antioxidant DPPH was the highest of the extracts tested. The results attributed the *T. chebula* extract with the highest oxygen radical absorption capacity (ORAC). In the FRAP assay, the extracts' ferric reducing antioxidant abilities were *T. arjuna, T. chebula and T. bellerica*. The methanol and water extracts of *Terminalia chebula* exhibit neuro- protective activities against H_2O_2 induced toxicity toward $PC1_2$ cells and are potential candidates for the treatment of H_2O_2induced neurodegenerative disease. The effective neuroprotective activity of the water extract is consequence of its OH and H_2O_2 scavenging activities, its greatest extraction yield and its total phenolic and tannin content[28].

Wound healing
Studies shows that the herbal paste preparation obtained from *Terminalia chebula* showed significant ($p<0.05$) improvement to stimulate fibroblast function, enhance synthesis of glycos aminoglycan's and deposition of collagen. Thus, it offers a distinct advantage to wound healing[29].

Analgesic and anti-inflammatory effect
The present study concludes that the ethanolic extract of *Terminalia chebula* fruits possesses analgesic and anti-inflammatory activities in mice and rats at the doses of 250 mg/kg and 500 mg/kg and, 300 mg/kg respectively[30].

VIBHITHAKI

Vibhithaki (*Terminalia belerica*) is distributed in plains and lower hills throughout India. It contains fructose, galactose, mannitol, beta sitosterol, gallic acid, chebulic acid, ellagic acid. It is indicated in jwara (fever), kasa (cough), swasa (asthma)[31].

Cardio protective, Anti -ulcer properties
The results of the present study indicate that the prior administration of the *Terminalia belerica* extract attenuates isoproterenol-induced MI. The cardio protective effect of the *Terminalia belerica* extract is probably related to its ability to strengthen the myocardial membrane by its membrane-stabilising action. *Terminalia belerica* extract at the dose level of 300 mg/kg was found to be more effective dose. In this study, the cardio protective potential of *Terminalia belerica* extract is evident.The anti-ulcer activity of ethanolic extract of *Terminalia belerica* fruits was investigated in pylorus ligation and ethanol induced ulcer models in wistar rats. The extract (250 mg/kg & 500 mg/kg) showed significant ($P<0.05$) reduction in free acidity and ulcer index in comparison to the control group[32].

Wound healing and anti- oxidant properties activity:
Studies have proved that the paste of *Terminalia belerica* have efficacy on wound healing. Herbal paste preparation of *Terminalia belerica* showed significant improvement on maturation, wound contraction and epithelialization in an experimental study. Crude aqueous extract of the fruits of *Terminalia belerica* have antioxidant properties since these contains enzymatic and non- enzymatic antioxidants, these can be very effective against microbes causing various diseases. In vitro assessment of the antioxidant activity of ethanolic fractions of the plant to scavenge 2, 2- Diphenyl-1-picrylhydrazyl (DPPH) and highly reactive hydroxyl radicals showed that the semi pure compounds present in the fractions are useful potential source of antioxidants[33].

AMALAKI

It can be seen throughout India. The main chemical constituents are Vitamin. C, phyllemblin, linoleic acid, indole acetic acid, corilagin, ellagic acid and phyllembic acid. It is indicated in prameha (diabetes mellitus), raktha pitta (bleeding disorder), netra roga (eye disease), kushta (skin disease) arsha (piles), etc[34].

Anti-inflammatory and analgesic activity
The anti-inflammatory and analgesic activities of the standardized water extract from the fruit of *Emblica officianalis* prepared according to the THP seem to be similar to NSAIDs rather than to steroidal drugs. Inhibitory effect on the synthesis and/or release of inflammatory or pain mediators may be the main mechanisms of action of P. emblica[35].

Antioxidant activity
Vitamin C, tannins and flavonoids present in amla have very powerful anti-oxidant activities, this help in elevation of hepatic anti-oxidant system and lowering of cytotoxic products[36].

Cardio- protective activity
Emblica officinalis fruit juice may be beneficial for the treatment of myocardial damage associated with type 1 diabetes mellitus. The activity of *Emblica officinalis* fruit juice can be attributed to the concentration of the polyphenol present. Results demonstrate the cardio protective potential of E. officinalis attributed to its potent antioxidant and free radical scavenging activity as evidenced by favorable improvement in hemodynamic, contractile function as well as tissue antioxidant status[37].

Anti-ulcer Activities
Methanolic extract of *Emblica officinalis* was studied against ulcer. *Emblica officinalis* had significant ulcer protective and healing effects and this might be due to its effects both on offensive and defensive mucosal factors[38].

Neuro protective activity
EO extract may be able to suppress oxidative stress of neuronal cells within the brain possibly indicating its neurotonic effects. EO seems to have a therapeutic potency possibly as alternative therapy for preventing or delaying progression of neurodegenerative diseases[39].

SUNTHI

Sunthi (*Zingiber officianale*) is distributed throughout India. It is indicated in sula (pain), amavata (rheumatoid arthritis), adhmana (distension of abdomen), athisara (diarrhoea), shlipada (filariasis), kasa (cough), swasa (asthma), hrudroga (heart disease), sopha (inflammation), arshas (piles), hikka (hiccough), etc[40].

Anti-oxidant activity
A study has proved that ginger extract is good source of polyphenolic compounds, including gingerols, shogaols, paradols

and gingerdions. It manifested a very good scavenging of ABTS radical cation and DPPH radical, respectively[41].

Anti-inflammatory, Analgesic activity
The rhizome extract of *Zingiber officianale* was investigated for anti-inflammatory and analgesic property in albino rats and mice respectively. The extract (50 and 100 mg/kg) produced significant inhibition of carrageenan induced rat paw oedema and reduction in the number of writhing induced by acetic acid in mice. The result shows that rhizome extract of *Zingiber officianale* possess anti-inflammatory and analgesic effect[42].

Cardio vascular effect
In vitro research indicates that gingerols and the related shogaols exhibit cardio depressant activity at low doses and cardio tonic properties at higher doses. Both shogaol and gingerol, and the gingerdiones, are reportedly potent enzymatic inhibitors of prostaglandin, thromboxane, and leukotriene biosynthesis[43].

Neuro proctective effect
Study have shown that *Z. officinale* is a neuro protectant. Dose-dependently enhances the memory with improvement in the locomotor and muscle grip strength in 3-NP-administered rats[44].

PIPPALI

It is found in hot parts of India. The chemical constituents are essential oil, sequiterpenes, caryopyllene, pipenonaline, pipercide, sesamin, beta sitosterol, piperine, 4, 5 dioxoaporphines. It is indicated in udara (ascites), pliharoga (spleenomegaly), jwara (fever), kushta, (skin disease) prameha (diabetes), etc [45].

Analgesic activity
Piper longum root has shown significant result as an opioid type analgesic in rat tail flick method and as a NSAID type analgesia using acetic acid writhing method. An aqueous suspension of *Piper longum* root powder given orally to mice and rat in doses of 200, 400, 800 mg/ kg. The delay in reaction time for thermal stimulus in rat and number of writhing to chemical stimulus in mice was detected in each group. The 400 and 800 mg/kg showed 50%protection against writhing[46]**.**

Anti-oxidant and anti-microbial properties
Study shows that the chloroform extract of *Piper longum* displayed the most effective in vitro antibacterial activity tested against *Micobacterium smegmatis* indicating their potential as a source of anti-mycobacterial drugs. Also, the chloroform extract exhibited greater amount of phenolic and had significant antioxidant activity compared to the hexane, ethyl acetate, ethanol, hydro ethanol and aqueous extracts. This validates the correlation of the total phenolic content of plant extracts with their antioxidant and antimicrobial properties[47].

Anti-inflammatory and Antiulcer activity
The fruit extract of *Piper longum* were reported to possess anti-inflammatory activity in carrageanan rat paw edema. And the piper extract and piperine possess inhibitory activities on prostaglandin and leukotrienes Cox-1 inhibitory effect and thus exhibit anti-inflammatory activity. The antiulcer activity was demonstrated by water decoction of ginger making up one of the constituents of Mahakasyaya drugs along with water decoction of *P. longum* and colloidal solution of *Ferula asafoetida* has been reported to protect against CRS, ASP and PL- induced gastric ulcers in rats. Piperine, an alkaloid of long peppers, inhibited gastric emptying (GE) of solids/liquids in rats and gastrointestinal transit (GT) in mice in a dose and time dependent manner. GE inhibitory activity of piperine is independent of gastric acid and pepsin secretion[48].

Cardio protective activity
Guineensine, isolated from chloroform extract inhibited ACAT activity in a dose dependent manner. An amide namely dehydropipernonaline having coronary vaso-relaxant activity was isolated from the fruit of *Piper longum*[49].

Neuro protective activity
PIP presented a neuro protective action, probably a consequence of its anti-inflammatory and antioxidant properties, making the drug a potential candidate for the treatment of neurodegenerative diseases[50].

MARICHA

Maricha can be found in hills of South western India. The main chemical constituents are piperene, piperethine, citronellol, cryptone, piperonal, camphene, beta alanine, carotene, ascorbic acid, pipercide[51].

Anti-oxidant, Analgesic and Anti -inflammatory activity
In vitro studies revealed that Piperine inhibited free radicals and reactive oxygen species, therefore known to possess protective effects against oxidative damage. The analgesic activities of both piperine and morphine in the tail flick assay were reversed on pre-treatment of animals with naloxone at dose of 5 mg/kg (i.p.). These results revealed the analgesic activity of piperine which possibly mediated via opioid pathway**.** The piperine was evaluated for the anti-inflammatory, analgesic, and anti-arthritic activities. The in vitro anti-inflammatory activities were evaluated on interleukin 1β stimulated fibroblast like synoviocytes obtained from rheumatoid arthritis[52].

HARIDRA

It contains curcumene, curcumenone, curcone, curdione, cineole, curzerenone, eugenol, camphene, camphor, borneol, curcumins. It is indicated in prameha, kushta, krimi, kandu, vrana, pandu[53].

Anti-inflammatory activity
Research study has shown curcumin to be a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation[54].

Analgesic activity
Different extracts of Curcuma longa at three doses 100, 200 and 400 mg/kg were evaluated for their analgesic activity using different animal models of analgesia. Shows significant analgesic activity in the tail flick test at 400 mg/kg one hour after administration[55].

Antioxidant activity
Curcuma longa exhibited highest antioxidant activity 74.61%. This activity could be attributed to both phenol and curcumin content. Moderate antioxidant activity is possible due to 95% oil content having major constituents, camphor, methyleugenol, pentadecanoic acid[56].

Cardio protective
Oral administration of Curcuma longa ethanolic or water extract (200 mg/kg) prior to doxorubicin produced a significant protection which was evidenced by significant reduction in mortality. Curcuma longa extracts renders resiliency against doxorubicin cardio toxicity due to their contents of poly phenolic compounds[57].

Neuro protective activity
Curcumin and manganese complex of curcumin are protective against vascular dementia[58].

DARUHARIDRA

It is mainly indicated in prameha (Diabetes mellitus), kushta (skin disease), netra roga (eye disease), kamala (jaundice) [59].

Anti-inflammatory activity
The ethanolic and aqueous extracts of *Berberis aristata* DC. Heartwood exhibited significant anti-inflammatory activity with percent inhibition 33.40% & 44.50% at a dose of 25 mg/kg, p.o. and 52.20% & 57.0% at a dose of 50 mg/kg, p.o., respectively. Whereas standard drug, Indomethacin showed an inhibition of 64.80%[60].

Anti-oxidant activity
The antioxidant activity of the methanolic extract were determined by DPPH (1, 1-Diphenyl-2-picryl hydrazyl) assay and Nitric oxide scavenging method[61].

PATA

It can be found throughout tropical and subtropical India. Chemical constituents are fangchinoline, cycleapeltine, cycleadrine, cycleacurine, cycleanorine, cycleahomine, chondocurine, magnoflorine[62].

Anti-oxidant activity
Phytochemicals present in the plants have strong antioxidant and anti-proliferative activities, Anti-oxidant activity. *Cyclea peltata* roots are reported to contain tetrandrine, a bisbenzyl isoquinoline dioxine alkaloid is well known for its antioxidant activity[63].

Ishvari
The plant is commonly known as snakeroot or birthwort and has been used traditionally for snakebite and postpartum infections respectively. According to Vagbhata after bloodletting the roots of nakuli are made into paste and can be applied in case of snake bite[64].

Analgesic and antioxidant activity
The plant extract showed dose dependent analgesic activity by acetic acid induced writhing inhibition in mice model. In the TLC-based qualitative antioxidant assay using 1, 1diphenyl-2-picryl hydrazyl (DPPH), the plant extract showed the free radical scavenging properties indicated by the presence of strong yellow spot on a purple background on the TLC plate[65].

Anti-inflammatory activity
Aristolochic acid also played a regulatory role in prostaglandin synthesis. It inhibited inflammation by both immunological and non-immunological agents. One mechanism of activity was thought to be as a direct inhibitor of phospholipase A2, decreasing the generation of eicosanoids and platelet-activating factors[66].

NEELINI

Major chemical constituents are a galactomannan, apigenin, kaempferol, tuteolin. It is used in udara (ascites), amavata (rheumatoid arthritis), jwara (fever). The fresh juice proved to be potential antidote on oral administration against cobra venom[67].

Anti-oxidant activity
A study shows that extracts exhibited 22-56% •OH scavenging activities at 250µg concentration in the reaction mixture and strong peroxidation inhibition against linoleic acid emulsion system (87-96%). The potential of multiple antioxidant activity of this plant is evident as the extracts possessed anti- hemolytic and metal ion chelating activities[68].

Analgesic activity
The analgesic activity of the ethanol extract of *Indigofera tinctoria* leaves (EEIT) was investigated in chemical models of nociception in mice. Suggest that the peripheral analgesic effect of *Indigofera tinctoria* may be attributed to inhibition of prostaglandin release and other mediators involved analgesic activity[69].

Anti-Inflammatory effect
The present study indicated that oral administration of ethanol extract of *I. tinctoria* dose dependently improve the potent anti-inflammatory activity. The extract lowers the carrageenan induced rat paw oedema[70].

AJAMOOTHRA

Goat urine balances all the three doshas. It mainly contains sodium chloride and urea. Due to katu and ushna guna it is kapha vata samaka and pitta samshodhana. It is krimighna (anti-bacterial), shothahara (anti-inflammatory), and vedanasthapana (analgesic). It is having lekhana (scrubbing), anulomana (downward movement), raktha sodhaka (blood purifier) property. It is indicated in rajayakshma (tuberculosis), udara roga (ascites), kushta (skin disease) and jwara (fever)[71].

ANTI -SNAKE VENOM ACTIVITIES OF DRUGS IN VISHA BILWADI

Amalaki
As Snake Venom Neutralizer EO and *Vitex negundo* were explored for the first time for anti-snake venom activity. No precipitating bands were formed between the snake venom and plant extract which confirmed that the plant extracts possess potent snake venom neutralizing capacity and need further investigation[72].

Pippali
A study has shown that piperine showed the anti-snake venom activities against Russell's viper venom in embryonated fertile chicken eggs, mice and rats by using various models. They found that administration of *P. longum* extract (PLE) and piperine significantly ($p<0.01$) inhibited venom induced lethality, haemorrhage, necrosis, defibrinogenation and inflammatory paw edema in mice in a dose dependent manner. PLE possesses good anti-snake venom properties and piperine is one of the compounds responsible for the effective venom neutralizing ability of the plant[73].

Haridra
Turmerone isolated from curcuma longa neutralize both haemorrhagic activity of bothrops venom and 70%lethal effect of crotalus venom in mice. It acts as an enzymatic inhibitor of venom with proteolytic activities[74].
Other than this, drugs like ishvari (*Aristalochia indica*), tulasi (*Ocimum sanctum*), sunthi (*Zingiber officianale*), vibhithaki (*Terminalia chebula*), neelini (*Indigofera tinctoria*), devadaru (*Cedrus deodara*), has shown ante venom activity[75].

Table 1: Ingredients of Visha Bilwadi Gutika

SN	Drug and Botanical name	Family name	Rasa	Guna	Veerya	Vipaka	Dosha karma
1	Bilva *Aegle marmalose*	Rutaceae	Kashaya Tiktha	Laghu, Rooksha	Ushna	Katu	Kapha vatahara
2	Tulsi *Ocimum santum*	Lamiaceae	Katu, Tiktha	Laghu Rooksha	Ushna	Katu	Kapha vatahara
3	Karanja *Pongamia pinnatta*	Fabaceae	Tiktha, Katu, Kashaya	Laghu Snigdha	Ushna	Katu	Kapha vatahara
4	Takara *Veleriana wallichi*	Valerianaceae	Tiktha, Katu, Kashaya	Laghu Snigdha	Ushna	Katu	Kapha vatahara
5	Devadaru *Cedrus deodera*	Pinaceae	Tiktha, Katu, Kashaya	Laghu Rooksha	Ushna	Katu	Kapha vatahara
6	Harithaki *Terminalia chebula*	Combretaceae	Pancha rasa except lavana	Laghu Rooksha	Ushna	Madhuraa	Tridoshahara
7	Vibhithaki *Terminalia bellerica*	Combretaceae	Kashaya	Laghu Rooksha	Ushna	Madhura	Kapha pittahara
8	Amalaki *Embelica officianalis*	Euphorbiaceae	Amla pradana pancha rasa	Laghu Rooksha	Sita	Madhura	Tridoshahara
9	Sunthi *Zingiber officianale*	Zingiberaceae	Katu	Guru, Rooksha	Ushna	Madhura	Kapha vatahara
10	Maricha *Piper nigrum*	Piperaceae	Katu	Laghu Rooksha	Ushna	Katu	Kapha vatahara
11	Pippali *Piper longum*	Piperaceae	Katu	Laghu Rooksha	Ushna	Madhura	Kapha vatahara
12	Haridra *Curcuma longa*	Scitaminaceae	Tiktha, Katu	Laghu Rooksha	Ushna	Katu	Kapha pittahara
13	Daruharidra *Berberis aristata*	Berberidaceae	Tiktha, Kashaya	Laghu Rooksha	Ushna	Katu	Kapha vatahara
14	Neeli *Indigofera tinctoria*	Fabaceae	Tiktha	Laghu Rooksha	Ushna	Katu	Kapha vatahara
15	Ishwari *Aristolochia indica*	Aristalochiaceae	Tiktha, Katu Kashaya	Laghu Rooksha	Ushna	Katu	Kapha vatahara
16	Pata *Cyclea peltata*	Menispermaceae	Tiktha	Laghu Rooksha	Ushna	Katu	Tridoshahara
17	Ajamoothra *Capra aegagrus hircus*		Katu, Lavana	Laghu Rooksha	Ushna	Katu	Kapha vatahara

Table 2: Properties of Ingredients in Visha Bilwadi Gutika

Hrudya	Shulahara	Shophahara	Vishahara	Kanduhara	Raktha dosha hara
Harithaki	Pippali	Tulasi	Tulasi	Tulasi	Tagara
Amalaki	Maricha	Karanja	Karanja	Karanja	
Sunthi	Sunthi	Devadaru	Tagara	Devadaru	
Pippali	Amalaki	Harithaki	Haridra	Haridra	
		Amalaki	Neeli	Daruharidra	
		Sunthi	Ishvari		
		Haridra	Pata		
		Daruharidra	Daruharidra		
		Pata	Maricha		

DISCUSSION

The usage of natural medicine has been influenced by inadequacy of biomedical health system, and due to its cost effectiveness and cultural acceptability. In India, the rural areas are most affected by snake envenomation and medicinal plants have been widely used as a remedy for treating snakebite. The ingredients of Visha Bilwadhi are having the action to treat venomous bites based on signs and symptoms especially in cobra bite and is widely practiced also. By virtue of its ushna virya, katu vipaka, kashaya, tikta rasa and kapha vata shaman properties, it is suitable for treatment of pain and swelling. The cobra bite is a neuro toxic poison, the studies shows that the drugs like tulasi, amalaki, haridra, pippali, tagara, sunthi, bilva, harithaki having neuro protective effect. Amalaki, neelini, devadaru, tulasi, ishvari, bilva, devadaru, sunthi, haridra having anti-venom properties it is essential for envenomation. The drugs like bilva, tulasi, karanja, tagara, harithaki, amalaki, sunthi, maricha, pippali, haridra, daruharidra and ishvari are having anti -inflammatory effect as the cobra bite produce swelling and pain first. Studies have shown that bilva, tulasi, karanja, tagara, harithaki, vibhithaki, amalaki, sunthi, maricha, pippali, haridra, neeli having analgesic properties. Bilva, tulasi, haridra, harithaki, vibhithaki, amalaki, sunthi, pippali are having cardio proctective activity also. After bite, there is chance of ulcer formation, tulasi, devadaru, harithaki, vibhithaki, pippali have wound healing property. This property will help if any ulcer form after bite. According to Ayurveda visha enters the body it will first affect the heart, so hrdayavarana is mentioned in our classics. In Visha Bilwadi drugs like harithaki, amalaki, sunthi, pippali have hrudya properties. Amalaki, sunthi, maricha, pippali are soolahara. Tulasi, karanja, devadharu, harithaki, amalaki, sunthi, haridra, daruharidra, pada are sophahara. Vishahara drugs are tulasi, karanja, tagara, ishvari, neelini, haridra, daruharidra and maricha. Kanduhara drugs are tulasi, karanja, devadharu, haridra and daruharidra. Tagara which is indicated in raktha pradushti, as the visha enters the body it will first vitiate blood. Devadaru which is one among vata prashamana dashaimani are also effective in darvikara (cobra) bite as

darvikara (cobra) bite is vata predominant. So, the combined action of all these drugs help in the management of darvikara bite.

CONCLUSION

Snake bite is one of the most common and many a times potentially fatal phenomenon. Anti -snake venom being the only therapeutic option available, but having many drawbacks, herbal plants provide a solid platform for the natural treatment of this serious issue. Data mentioned above clearly said that the herbal medications have excellent potential to treat snake bite. Herbal medicinal plants are an important element of indigenous medical systems globally. The usage of natural medicine has been influenced by inadequacy of biomedical health system, and due to its cost effectiveness and cultural acceptability. In India, the rural areas are most affected by snake envenomation and medicinal plants have been widely used as a remedy for treating snakebite. Plant extracts represent an extremely rich source of pharmacologically active compounds and possess more than one biochemical/pharmacological property. Interaction of such compounds with the toxins/enzymes leads to the neutralization/inhibition of their activities. Most of the ingredients of visha bilwadi gutika have ante snake venom and neuro protective action which help to reduce the mortality rate. The anti-inflammatory, analgesic, anti-microbial properties of the drugs reduce the severity of the symptoms also. Many of the drugs have vishagna and hrudha action also. Thus, Visha Bilwadi gutika can be given in darvikara (cobra) bite.

REFERENCES

1. Rajeev sason, Plants used in treatment of snakebite by the tribal communities of Paschim Medinipur district, West Bengal 2013 Review Article - wjpls, 2016, Vol. 2, Issue 4, 464-470
2. Vv pillai, modern medical toxicology completely updated, revised profusely illustrated, jaypee brothers medical publisher(p)LTD,4th edition, p146
3. VM. kuttikrishna menon, kriya kaumadhi a Malayalam treatise on ayurvedic toxicology p274
4. Rajveer sason, Conceptual study on antitoxic effect of bilwadi gutika,WJPLS 2016
5. https://en.wikipedia.org,date:15/2/2017
6. Neeta singh, Antioxidant and phytochemical study of aegle marmelos fruits and root-international journal of pharmaceutical science,2014
7. Vengal rao, Evaluation of neuro-proctective activity of aegle marmelos against sodium nitrate induced neurotoxicity in albino rats, international journal of innovative pharmaceutical research 2014
8. Asha jhjhria Krishna kumar, Tremendous pharmacological values of aegle marmelos, international pharmaceutical science review and research-2016
9. Asha jhjhria, Krishna kumar, Tremendous pharmacological values of aegle marmelos, international pharmaceutical science review and research-2016
10. https:/enwikipedia.org, date 15/2/2017
11. Kandaswamy selvan, rathika rajikanth, Anti-oxidant and secondary metabolites in o. santum at various habits, journal of medicinal plants research 2013
12. Reema rathore, An experimental study of analgesic effect of medicinal plants tulsi (ocimum santum),ethno medicine,2013
13. Mrutynjajmmirje,Evaluation of the anti -inflammatory activity of ocimum sanctum in albino rats, international journal of current microbiology and applied science,2014
14. Shahedor rabman, Ocimum sanctum a review of phytochemical and pharmacological profile, American journal of drug discovery and development,2011
15. Shahedor rabman, Ocimum sanctum a review of phytochemical and pharmacological profile, American journal of drug discovery and development,2011
16. JLN sastry, dravya guna vijnana,3rd edition, vol 2, chaukhambha orientalia Varanasi 2008, p168
17. Maniganesh, mani vasudevan, kalippan, Anti -inflammatory and analgesic effect of pongamia glabra leaf gall extracts, pharmacologyonline,2008
18. Zahid iqbal sajid, farooq, answae, Anti -oxidant, anti-microbial properties of phenolic extracts of different solvent extracts from bark leaves and seed of Pongamia pinnatta, open access molecules,2012
19. JLN sastry,d ravya guna vijnana,3rd edition,vol 2,chaukhambha orientalia Varanasi 2008, p801
20. Sp sah, cs mathela, valeriana wallichi-antinociceptive studies on experimental animal models and possible mechanism of action, pharmacologia,2012
21. Sudhanshan, nidhi, Evaluation of anti- oxidant properties of Valeriana wallichi to scavenge free radicals, Asian journal of pharmaceutical and clinical research, 2012
22. Dr supriya priyambada, dr jagadheesh, Dose dependent anti-inflammatory effect of Valeriana wallichi in 0.1 MI of 1% carrageenan induced hind paw edema in male albino rats,journal of pharmacy and biological science 2015
23. JLN sastry, dravya guna vijnana,3rd edition,vol 2,chaukhambha orientalia Varanasi 2008, p506
24. Sumeel guptha, anu walia, Phytochemistry and pharmacology of Cedrus deodera: an over view, International journal of pharmaceutical science and research,2011
25. Sumeel guptha, anu walia, Phytochemistry and pharmacology of Cedrus deodera:an over view, International journal of pharmaceutical science and research,2011
26. JLN sastry, dravya guna vijnana,3rd edition,vol 2,chaukhambha orientalia Varanasi 2008, p210
27. Vidhya unnikrishnan, k nishetwar, Cardio protective activities of herbal formulation of bhava Mishra-a review,IAMJ
28. Aditya arya, shait nyanthulla,Anti -oxidant and hypoglycemic activities of leaf extract of three popular Terminalia species, e journal of chemistry,2012
29. Aparna upadhayay, pooja agrahari, a review on the pharmacological aspects of terminalia chebula, science alert-an open acess publisher
30. Md sagkanth ibne, zakia sultana, Evaluation of analgesic and anti- inflammatory activities of ethnolic extract of Terminalia chebula fruit in experimental animal models, American journal of plant science 2014
31. JLN sastry, dravya guna vijnana,3rd edition, vol 2, chaukhambha orientalia Varanasi 2008 P218
32. Alam firoj, Siddiqui.h, cardio protective activity of Terminalia bellerica on isoprenaline induced myocardial necrosis in rats, Asian journal of chemical and pharmaceutical research 2014
33. Alam firoj, Siddiqui.h, cardio protective activity of Terminalia bellerica on isoprenaline induced myocardial necrosis in rats, Asian journal of chemical and pharmaceutical research 2014
34. JLN sastry, dravya guna vijnana, 3rd edition, vol 2, chaukhambha orientalia Varanasi 2008 P222
35. Anti- inflammatory and analgesic activities of water extract from the fruit of Phyllanthus embelica, international journal of applied research in natural products 2010
36. Madhuri.s, pandey govind, Anti- oxidant immune modulatory and anti- cancer activities of Embelica officianalis :An over view, international research journal of pharmacy,2011
37. Prusan R Bhandari, Embelica officinalis A review of potential therapeutic applications, international journal of green pharmacy,2012

38. R.jain, r.pandey, A review on medicinal importance of Emblica officinalis, international journal of pharmaceutical science and research2015
39. Rankrishna, preethiguptha, Neuro protective effect of Emblica officinalis extract against H2O2 induced DNA damage and repair in neuroblastoma cells, journal of homeopathy and ayurvedic medicine an open asses journal,2014
40. JLN sastry, dravya guna vijnana,3rd edition, vol 2, chaukhambha orientalia Varanasi 2008 P519
41. Silvia mosovka, dominika, Anti -oxidant activity of ginger extract and identification of its active component,2015
42. Raji.Y, Udoh, Anti -inflammatory and analgesic properties of the rhizome extract of Zingiber officinale, African journal of biomedical research,2002
43. Rajesh kumar Mishra, Anil kumar,asok kumar, Pharmacological activity of Zingiber officinale ,International journal of pharmaceutical and chemical science 2012
44. Manisha sharma, nidhi sharma, Neuro protective effect of Zingiber officinale in 3np induced Huntington disease, journal of pharmacy,2012
45. JLN sastry,dravya guna vijnana,3rd edition,vol 2,chaukhambha orientalia Varanasi 2008P953
46. G vedhanayak, geetha u, alice kuruvila, Analgesic activity of Piper longum root, indian journal of experimental biology 2003
47. Baraa.cc,singh a sens ,In vitro antioxidant and anti -bacterial activity of seed of piper longum: a comparative study SAJ pharmacy and pharmacology,2014
48. Dhana lakshmiumamaheswari, Phyto chemistry and pharmacology of piper longum, a systemic review, world journal of pharmaceutical science,2016
49. Mitreyi zaveri, Amit khandar, Chemistry and pharmacology of piper longum, international journal of pharmaceutical science,2010
50. Alyne oliveria correia,alilio augusto pinnetel cruz, Neuroprotective effect of piperine an alkaloid from piper genus on parkinsons disease model in rats, journal of neurology and therapeutics,2015
51. JLN sastry, dravya guna vijnana,3rd edition, vol 2,chaukhambha orientalia Varanasi 2008 P450
52. Katina suhana Andrade, Sandra regina, Anti -oxidant activity of black pepper oil-obtained by superficial co2, oberoamerican conference on supercritical thids cartagena de Indians 2013
53. JLN sastry, dravya guna vijnana,3rd edition, vol 2, chaukhambha orientalia Varanasi 2008 P514
54. Julies juneka, Anti -inflammatory properties of curcumin, A major constituent of curcuma longa:A review of preclinical and clinical research, alternative medicine review,2009
55. S.john,s nikil, Analgesic property of different extract of curcuma longa: an experimental study in animals journal of natural remedies,2009
56. Gayathri nayak,rajani kantasahu, Evaluation of anti- oxidant activity of ethnolic extract of five curcuma species, International journal of pharmacy,2011
57. Eman m,amal,ahd elazeen,abeer, Cardioprotective effect of curcuma longa extract against doxorubic induced cardio toxicity in rats, journal of medicinal plants research 2011
58. Ishita chattopadhyay, kaushik Biswas, Turmeric and curcumin: biological actions and medicinal applications, current science 2004
59. JLN Sastry, dravya guna vijnana,3rd edition,vol 2,chaukhambha orientalia Varanasi 2008 P55
60. Vijender singh, gunjan, deepthi katiyar, anti- inflammatory activity of alcoholoic and aqueous heart wood extract of Berberis aristata, Asian journal of pharmaceutical and clinical research,2014
61. Ovas dar, Reena Lawrence HPLC, anti- oxidant and anti-bacterial activities of methanolic extract of Berberis aristata stem, International journal of science and research,2014
62. JLN sastry, dravya guna vijnana,3rd edition,v ol 2,chaukhambha orientalia Varanasi 2008 P51
63. Suman singh, Niteswar, Review on Cissampelos pariera and Cyclea peltata(pata dwaya) phytopharmacological perspective,International journal of ayurvedic medicine,2013
64. JLN sastry, dravya guna vijnana,3rd edition,vol 2,chaukhambha orientalia Varanasi 2008 P91
65. Farhana Yasmin, Mahim Hossain,amit sardaranalgesic, anti-diarrheal, anti -oxidant, cytotoxic and oral glucose tolerance activities of ethnolic leaf extract of Aristalochia indica, bioscience and bioengineering communications,201
66. Aristalochia indica: A review of literature
67. JLN sastry, dravya guna vijnana,3rd edition,vol 2,chaukhambha orientalia Varanasi 2008 P698
68. nagarajan, sellamuttu manian, anti -oxidant and free radical scavenging potential of different solvent extract of Indigifera tinctoria leaves, International journal of pharmacy and pharmaceutical science,201
69. B.R Sarkar,V.K raj,B Kapoor sharma , Preliminary phytochemical screening and evaluation of anti-inflammatory activity of ethnolic extract of leaves of Indigofera tinctoria, International journal of research in phytochemistry and pharmacology,201
70. Saraswathi motamarri, karthikeyan, rajeshwari, Indigofera tinctoria-a phytopharmacological review,international journal of research in pharmaceutical and biomedical science,2012
71. https//www.slideshare.net, Date:2/2/2017
72. Jayaweera, D.M.A.: Medicinal Plants used in Ceylon Part 2. National Science Council of Sri Lanka. Colombo 1980.
73. Shenoy PA, Nipate SS, Sonpetkar JM et al. (2013). Anti-snake venom activities of ethanolic extract of fruits of Piper longum L. (Piperaceae) against Russell's viper venom: Characterization of piperine as active principle. Journal of Ethnopharmacology. 147(2): 373-382.
74. ferreira, LAF, Herniques, OB andreoni, AAS, vital GRF campos MMC, haber mehl, GG and moraces, VLG,antevenom and biological effect at turmerone isolated from curcuma longa, toxicon 1999
75. Muhammad hassan, antivenom potential of Pakistani medical plants, inhibition of coagulation activity of najgaja karchiensis toxin, current science 2013

Cite this article as:

G. Sunitha and Gazala Hussain. Visha bilwadi gutika: A review. Int. J. Res. Ayurveda Pharm. 2017;8(Suppl 2):42-49 http://dx.doi.org/10.7897/2277-4343.08281

Source of support: Nil, Conflict of interest: None Declared