WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 17, 1052-1064. Review Article ISSN 2277–7105

SCIENTIFIC BASIS OF SHARAPUNKHA PRAYOGA IN ALARKA VISHA W.S.R TO RABIES – A REVIEW ARTICLE

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Article Received on
18 July 2024,

Revised on 08 August 2024,
Accepted on 28 August 2024

DOI: 10.20959/wjpr202417-33729

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ABSTRACT

Alarka Visha mentioned in the Samhita is mainly the disease which affects the *Sanjna vaha Srotas*. Even though there is no direct correlation of *Alarka Visha* in modern science; most of the symptoms are seen in the Rabies. Rabies is a zoonotic disease of warm-blooded animals such as dogs, jackals and wolves, transmitted to man by bites or lick, also it is an acute viral disease caused by type-1 Lyssa virus. India has been reported as having highest rabies cases in the world. According to WHO, there are approximately 10 million cases of rabies get reported every year and about 55000 deaths. Many treatment protocols have been mentioned by Acharyas, *Sharapunkha Prayoga* is one among them. Present paper includes the probable mode of action of *Sharapunkha Prayoga* and the chemical constituents in the treatment of *Alarka Visha* with respect to Rabies disease and its need in research field.

KEYWORDS: *alarka visha*, rabies, *sharapunkha*.

INTRODUCTION

Agada tantra is one among *Ashtanga Ayurveda* mainly concerned with the study of poison, its action, identification and management. *Visha* includes *Sthavara, Jangama and Krithrima. Alarka visha* which has been mentioned under the *Jangama visha* by *Acharyas* which is caused by the bite of *Shwa*(dog), *Shrugala* (fox), *Taraksha* (jackal), *Vruksha*(hyena) *Vyagra* (tiger) as per *Sushruta Samhita* and *Astanga hridaya*.[1,2] According to the modern view,

most of the symptoms along with the cause indicates its resemblance to the Rabies. Rabies is an acute, highly fatal viral disease caused by the Lyssa virus present in the affected animals. Rabies virus mainly transmitted to the human body through the bite or lick of an infected animals where the saliva infiltrated with the virus.

Rabies is a fatal disease in developed as well as developing countries including India. The virus reaches the brain from the bite site through cognate sources and leads to the inflammation, loss of sensation, causing the animal to run a lot, hanging tail, lower jaw and shoulder, excessive salivation, become deaf and blind. Disease is mainly characterised by encephalitis with spasm of different muscles, paralysis, hydrophobia etc.[3]

Types of rabies

1. Furious rabies – it accounts for 80% of total cases, manifests painful spasm of the pharynx and larynx, hypersalivation, hyperactivity, hydrophobia sometimes aerophobia with aggressive behaviour.[4]
2. Paralytic rabies: paralysis of involved limbs, ascending palsy to involve muscle of respiration and deglutition.[5]

Alarka visha

According to *Charaka*, it is due to the vitiation of *Tridosha* and *Rasadi dhatu* caused by dog bite.[6]

According to the *Sushruta* and *Vagbhata*, when *Vata* gets aggravated in the body of dog, fox, jackals, hyena, tiger etc, it combines with the aggravated *Kapha* and accumulates in the channels of their sense organs and causes loss of sensation or hampers the consciousness.[7,8]

Pathogenesis of rabies[9]

Rabies is caused by a neurotropic virus of family *Rhabdoviridae*, genus Lyssa virus. Animal which got infected with Lyssa virus is able to transmit the disease to the human through the infected saliva into the blood stream by bite or lick or to any membrane (eyes, nose and mouth).

When the virus is

1. Introduced through bite, it replicates in the skin or muscle and enters into the peripheral nervous system.

2. It passes to the chain of nerve cells towards central nervous system. Though a small amount of virus could enter the blood stream, it is not considered infected as the virus is unable to replicate in the blood.
3. The incubatory period is the time taken by the virus to move from the bite site to the brain.
4. Incubation period ranges from 2 weeks to several months, moreover the distance of bite wound from the brain determine the length of incubation.
5. When the virus enters the central nervous system, it affects the nearby salivary glands where in replicates and shed in the saliva.
6. It then spreads centrifugally to numerous other organs.
7. The virus affects the brain functions causes the unexplained aggression, impaired locomotion, varying degree of paralysis, extreme depression and viciousness.

Ingredients of *Sharapunkha Prayoga*[10]

1. Root of *Sharapunkha* – 1 *Karsha*
2. Root of *Datura* – ½ *Karsha*
3. *Tandula* – required quantity

Method of preparation and administration

1. Root of *Sharapunkha* and *Datura* macerated using *Tandulodaka* and made into paste form.
2. The ball of paste enveloped with leaves of *Datura* and pan cake is prepared out of it.
3. It is consumed at the time of meals by the rabies infected person.
4. The treatment should be done for 3-5 days.

UNDERSTANDING THE EFFECT OF CHEMICAL COMPONENTS OF THE INGREDIENTS IN CURING THE DISEASE

1. *SHARAPUNKHA*

Scientific name – *Tephrosia purpurea. linn.*

Family – Fabaceae

The herb is found abundant as a weed in places like river beds, roadside etc., this plant has been referred as "*Sarwavrana Vishapaha*"[11] which means it is having the property to heal the wound as well as used in the condition of poison. The plant possesses anti-inflammatory, analgesic, antipyretic, anticancer, hypoglycaemic, immunomodulatory, antioxidant action, antimicrobial.[12]

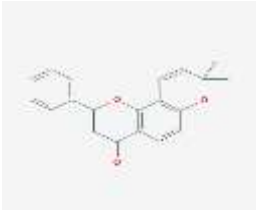
CHEMICAL COMPOUNDS OF *SHARAPUNKHA* ROOT ARE

A. (-)-Isolonchocarpin[13]

It is a flavonoid first isolated from the root extract of *Tephrosia purpurea*

Molecular formula – $C_{20}H_{18}0_3$

Chemical Structure.[14]



Before oral absorption, flavonoids undergo DE glycosylation either by lactase phlorizin hydrolase or cytosolic beta-glucosides. The absorbed aglycone is then conjugated by methylation, sulphatation or glucuronidation. Both the aglycones and conjugates can pass the blood brain barrier.

In the CNS several flavones bind to the benzodiazepine site of $GABA_A$ receptor resulting in sedation, anxiolytic or anticonvulsive effects.

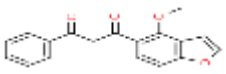
Flavanols protect the nerve injuries and acts as free radical scavengers with antioxidant activity.

It has become clear that flavonoids play a role in enzyme and receptor system of the brain, exerting various effect on central nervous system including the neurodegeneration.

B. Pongamol

Molecular formula- $C_{18}H_{14}0_4$

Chemical Structure.[15]



It is a flavonoid exhibit numerous pharmacological property.[16]

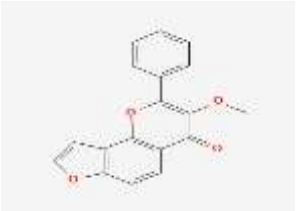
Sub-acute toxicological study of pongamol where the pongamol isolated from the seeds of the plant *Pongamia pinnata* revealed its anti-convulsant effect[17], CNS depressant activity[18] were reported.

C. Karanjin

It is a furanoflavonol, a type of flavonoid.[19]

Molecular formula-$C_{18}H_{12}O_4$

Chemical Structure[20]

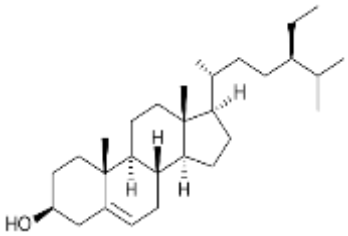


Research study revealed the information that Karanjin which is extracted from seeds of *Pongamia pinnata* inhibits oxidative stress[21] and showed antioxidant activity and tissue protecting activity.[22,23]

D. β – sitosterol

Molecular formula-$C_{29}H_{50}O$

Chemical Structure[24]



β-sitosterol belongs to the group of phytosterols, which are active trace components.

Research carried out on β -sitosterol reduces anxiety and synergises with establishing anxiolytic drugs in mice.[25]

Research carried out where beta sitosterol alleviates inflammatory response via inhibiting the activation of ERK/p38 (Extracellular signal-regulated kinase) in LPS(Lipopolysaccharide)-Exposed BV-2 cells.[26]

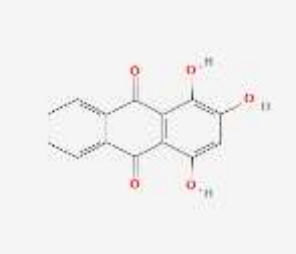
Study revealed that inflammatory response illustrated that β-sitosterol treatment can reduce the LPS-induced expression of inflammatory mediators (interlukin-6), inducible nitric oxide (iNOS), tumour necrosis factor-α (TNF α) and cyclo -oxygenase 2 (COX-2). The related signalling pathway analysis demonstrated that β-sitosterol treatment can inhibit the LPS-induced activation of p38 pathway.[27]

E. Purpurin

Purpurin is a trihydroxyanthroquinone derived from anthracene

Molecular formula-$C_{14}H_8O_5$

Chemical structure[28]



Purpurin has various effects, including anti-inflammatory effects, and can efficiently cross the blood brain barrier. The investigation of purpurin effect on oxidative stress in HT22 cells and mild brain damage in gerbil hippocampus CA1 region induced by transient forebrain ischemia showed positive result.

Treatment with purpurin significantly reduces phosphorylation of JNK, ERK/p38 signalling in HT22 cells.

It also significantly decreases the activation of microglia and astrocytes. It suggests that purpurin can be one of the potential candidates to reduce neuronal damage and inflammatory responses after oxidative stress in ischaemic change in gerbil.[29]

2. DATURA

Scientific name – *Datura metel. Linn.*

Family – *Solanaceae*

Research work showed the potential in-vitro anti-rabies activity of *datura metel* in Vero (African green monkey canine kidney) cell line which was determined by REFIT method and PCR method.[30]

Chemical composition of datura root

A. Hyoscine

Molecular formula-C17H21NO4

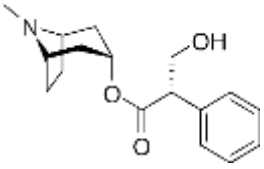
Chemical Structure[31]

Research study carried out on central nervous system effects of Hyoscine in man showed – by injecting 0.15-0.8 mg, hyoscine subcutaneously in 54 subjects induced bradycardia and marked decrease in salivation. The effect was maximum for the period of 2 hours after administration.[32]

B. Hyoscyamine

Molecular formula-$C_{17}H_{23}NO_3$

Chemical Structure[33]



Hyoscyamine is a natural anticholinergic agent

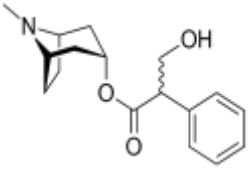
It is a main alkaloid which is levo form of atropine

It also shows sedative property (mors et al. 2000)[34]

C. Atropine

Molecular formula-$C_{17}H_{23}NO_3$

Chemical Structure[35]



Atropine It is a muscarine antagonists, which is used to treat Parkinson's disease and parasympathetic stimulation of the eye, heart, urinary, respiratory and gastrointestinal tract.

Atropine and scopolamine are class of compounds that inhibit parasympathetic nerve impulses by selectively blocking the binding of the neurotransmitter acetylcholine to its receptor in nerve cells.[36]

Atropine also reported to have an antiviral activity, it inhibits the growth of enveloped virus such as herpes simplex virus, new castle disease virus, sindbis, vaccinia, adenovirus and Japanese encephalitis virus.[37]

Atropine also blocks the glycosylation of viral proteins herpes virus and hence the production of new infection virus particles(virions).[38]

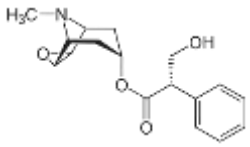
Atropine prevent the recurrent severe spasm due to the attempt to swallow the accumulated saliva in the mouth cavity.[39]

Extra neuronal involvement has been documented where the cardiac structure involved which play a major role in severity of the disease leads to myocarditis and cardiac arrhythmias. Atropine is helpful in case of brady arrhythmias.[40]

D. Scopolamine

Molecular formula-$C_{17}H_{21}NO_4$

Chemical Structure[41]



Scopolamine is an anticholinergic agent which is helpful in excessive salivation.

New research study showed that single dose of the compound called scopolamine called scopolamine hydrobromide inactivates rabies virus.[42]

DISCUSSION

Alarka visha which is mentioned under *Jangama visha* having many treatment protocols mentioned under this. One among them is *Sharapunkha prayoga* where we can consider the *Prativisha prayoga* concept where datura (*Sthavara visha*) is one of the ingredients to cure *Alarka visha (Jangama visha).* According to *Bhavaprakasha*, *Datura* and *Sharapunkha* are *Vishapaha* (anti-poisonous) the effect enhances when both the drugs used together.

In modern aspect, symptoms of *Alarka visha* correlated to that of rabies. Rabies is a major health hazard which is affecting the vast population. Rabies virus infect neurons with neuro-

invasiveness and neurotropism which is being the major defined characteristic in pathogenesis of a classic rabies infection (Gnanadurai et al. 2015).

As the rabies virus which affects the central nervous system, it is noted that the medications must pass through the BBB (blood brain barrier), the flavonoids which is present in the root of *Sharapunkha* undergo DE glycosylation either by lactase phlorizin hydrolase or cytosolic beta-glucosides. The absorbed aglycone is then conjugated by methylation, sulphatation or glucuronidation. Both the aglycones and conjugates can pass the blood brain barrier. Thereby it binds to the benzodiazepine site of $GABA_A$ receptor resulting in sedation, anxiolytic or anticonvulsive effects. Flavanols inhibit the nerve inflammation and prevent neuronal damage and also act as free radical scavengers with antioxidant activity. It has become clear that flavonoids play a role in enzyme and receptor system of the brain, exerting various effect on central nervous system including the neurodegeneration.

One among the symptoms of rabies encephalitis is recurrent convulsions, where the pongamol give anti-convulsant effect also with CNS depressant activity.

Oxidative stress which is the main problem in the rabies affected individuals leads to the neuronal progress degeneration.[43] Oxidative stress induces overproduction of reactive oxygen species and reactive nitrogen species; this type of molecules damage protein, lipid and nucleic acid.[44,45,46] Brain tissues are extremely sensitive to the oxidative stress due to its high oxygen consumption, iron content, polyunsaturated fatty acids and low antioxidant capacity.[47,48] Moreover, hippocampus and amygdala is more sensitive to oxidative injury.[49] karanjin inhibits oxidative stress and showed antioxidant activity and thereby attains tissue protecting activity.

The progression of rabies symptoms leads to anxiety. Research carried out on β -sitosterol reduces anxiety.

Infection with street RABV strain induces the phosphorylation of p38, JNK (c-Jun N-terminal kinase) AND ERK (extracellular signal regulation kinase) in human. Research carried out where beta sitosterol alleviates inflammatory response via inhibiting the activation of ERK/p38 (Extracellular signal-regulated kinase) in LPS(Lipopolysaccharide)-Exposed BV-2 cells.[50]

Microglia plays a crucial role during virus pathogenesis in the central nervous system. research study revealed that differentially expressed genes from the microglial cells after RABV infection were mainly involved in innate immune responses, inflammatory response and host antiviral response[51] purpurin decreases the activation of microglia and astrocytes.

Scopolamine and atropine inhibit the excessive salivation and study shows atropine is having antiviral activity and scopolamine hydrobromide inactivates rabies virus.

CONCLUSION

Ayurveda emphasizes preventive and curative aspect of almost all the diseases. One among them is *Sharapunkha Prayoga* where the chemical compositions such as – (-) *isolonchocarpine, pongamol, karanjin, β-sitosterol, purpurin, hyoscine, hyoscyamine, atropine, scopolamine* may play better role in order to cure rabies. Fortunately, rabies is 100% preventable disease; unfortunate lies in its 100% mortality if it enters CNS. Present paper emphasizes the need of study to prove the efficacy of the ayurveda remedies in curing the fatal diseases and to prove its precious gift to the medical science.

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