EVALUATION OF EFFECT OF HYDROALCOHOLIC EXTRACT OF CASSIA FISTULA LINN AGAINST NEUROPATHIC PAIN

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ABSTRACT

Cassia fistula is widely grown as an ornamental plant in tropical and subtropical areas. Hydroalcoholic extract of Cassia fistula Linn leaf were assayed in wistar, strain albino rats. The extracts were found to possess significant neuropathy activity. In the present investigation, the rats were exposed to alcohol & acrylamide induced peripheral neuropathy in dose dependent manner. Cassia fistula leaf was unable to protect the animals from acrylamide while it was able to reverse the alcohol induced peripheral neuropathy in dose dependent manner in the rats. The results suggest that Cassia fistula could be of immense importance in the amelioration of the mono neuropathy in the human beings.

KEY WORDS: Cassia fistula, Neuropathic pain.

INTRODUCTION

Pain, an unpleasant sensation that we all experience in daily life, is an alert mechanism to prevent further or impending tissue injury. Acute pain rarely needs medical attention; when it does, non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, more powerful opioids analgesics, or local anesthetics can adequately control the pain. Almost all currently used analgesics were initially developed for acute pain. Chronic pain differs from acute pain not only in its onset and duration, but more importantly in the underlying mechanisms. Chronic pain may not have identifiable ongoing injury or inflammation, and often responds poorly to NSAIDs and opioids. Better treatment of chronic pain will require clear understanding of what leads to such persistent pain, and testing of pharmacological agents in such settings. Animal models can provide useful and essential systems to study chronic pain. Numerous animal models have been developed to simulate specific human painful conditions, mostly by producing diseases or traumatic injuries that have painful sequellae.

Neuropathic pain and Cancer pain are two of the most difficult types of pain to treat. Neuropathic pain, defined as 'pain initiated or caused by a primary lesion or dysfunction of the nervous system, is probably not the result of a single pathophysiological mechanism, but rather the final product of altered peripheral, spinal and supraspinal processing. Persistent Neuropathic pain is associated with severe sleep and mood disturbances (such as depression or anxiety) that interfere with physical, social, work and emotional well-being. Neuropathic pain may result from disorders of the peripheral nervous system or the central nervous system (brain and spinal cord). Thus, neuropathic pain may be divided into peripheral neuropathic pain, central neuropathic pain, or mixed (peripheral and central) neuropathic pain. Native to India, the Amazon and Srilanka, Cassia fistula Linn., a semi-wild Indian Labrum also known as the Golden Shower, has become extensively diffused in various countries including Mauritius, India, South Africa, Mexico, China, West Indies, East Africa and Brazil as an Ornamental tree for its beautiful bunches of yellow flowers. Main chemical components are anthraquinones, fistulic acid , rhein, rheinglucoside, sennosides A and B, plobaphenes, emodin, chrysophanic acid, fistuacacidin, lupeol, beta-
sitosterol and hexacosanol. A tropical ornamental tree with a trunk consisting of hard reddish wood, growing up to 40 feet tall. The wood is hard and heavy. It has showy racemes, with bright, yellow, fragrant flowers. Cassia fistula’s laxative actions come from a group of well-documented compounds called anthraquinones that are found in all Cassia plants in varying degrees. The seeds contain approximately 2% anthraquinones, 24% crude protein, 4.5% crude fat, 6.5% crude fiber, and 50% carbohydrates. The leaves have been documented with 15.88% crude protein, 6.65% crude fat, 20% crude fiber, and 39.86% carbohydrates.

MATERIALS AND METHODS

Collection and extraction of Plant material

The leaf of *Cassia fistula* was collected from Agricultural College Pune and authentified at Botanical Survey of India, Pune (No. BSI/WC/tech/2009/621). The plant leaves were air dried and converted into the powder by mechanical grinder. The leaf powder was stored in tightly closed glass jar. The extraction procedure was carried out by cold maceration using pure 10% v/v ethanol in water as solvent. The extract was concentrated under air at 65°C. It was stored in cool place and reconstituted in distilled water using TWEEN 20 as suspending agent just before use.

Animals

Adult Male & Female (Wistar strain) rats (125–150 g) were procured from Laboratory Animals Resource Section of Indian Veterinary Research Institute were used for the present study. The experimental procedures were approved by Animal Ethics Committee. The animals were housed in groups of 5–6 in polypropylene cages 7 days prior to surgical procedure, so as to acclimatize to the laboratory conditions. The animals had free access Balanced rat feed and standard pellet chow throughout the experimental protocol & provided ad libitum along with all necessary care throughout the experimentation. The rats were kept at room temperature of 25±2 °C with relative humidity of 45-55% and 12:12 h dark/light cycle.

Acute Toxicity Test

Acute toxicity study was performed in mice according to O.E.C.D. guidelines. The extracts were administered intraperitoneally (i.p.) at doses of 175, 550, 2000 mg/kg. They were then observed for signs of toxicity, continuously for 2 h, and for mortality up to 24 h & 48 h, after injection.

Experimental set up

Six groups, each comprising six wistar–albino rats, were employed in the present study.

Group I (normal control group): Rats were not subjected to any surgical procedure and were kept for 14 days. Behavioral tests were carried out to assess noxious threshold and motor coordination, on certain day intervals, i.e., day 1, 3, 5, 7, 10, 12, 14…28.

Group II (axotomy control group): Rats were subjected to surgical procedure to isolate and transect left sciatic nerve. Behavioral tests were assessed as described in group II.

Group III (vehicle treated group): After subjecting the rats to axotomy, TWEEN 20 was administered orally for 10 consecutive days, starting from the day of surgery. Behavioral tests and parameters were assessed as described in group II.

Group IV (*Cassia fistula* treated group, 50 mg/kg): After subjecting the rats to axotomy, hydroalcoholic extract of *Cassia fistula* (50 mg/kg p.o.) was administered for 28 consecutive days, starting from the day of surgery. Behavioral tests and parameters were assessed as described in group II.

Group V (*Cassia fistula* treated group, 100mg/kg): After subjecting the rats to axotomy, hydroalcoholic extract of *Cassia fistula* (100 mg/kg p.o.) was administered for 28 consecutive days, starting from the day of surgery. Behavioral tests and parameters were assessed as described in group II.

Group VI (*Cassia fistula* treated group, 200mg/kg): After subjecting the rats to axotomy, hydroalcoholic extract of *Cassia fistula* (200 mg/kg p.o.) was administered for 28 consecutive days, starting from the day of surgery. Behavioral tests and parameters were assessed as described in group II.

Assessment of neuropathic pain in rats:

Acryllamide Induced Neurotoxicity: Acryllamide was administered at a dose of 50 mg/kg for 1 week. After the induction of neuropathy, treatment were initiated and continued for 28 days.
Alcohol induced neuropathy: Ethanol was administered at dose of 12%v/v (4mg/kg/day) for a period of 15 days. After the induction of neuropathy, treatment were initiated and continued for 28 days.\textsuperscript{12}

Parameters and Tests

Motor coordination test: Motor coordination will be evaluated by a Rota-Rod device as described by Jones and Roberts (1968). Rats will be placed for 1min on the rotating rod. The time taken for the falling from the roller, during 1min, will be recorded.\textsuperscript{13}

Tail Immersion Test: The tail of the rat will be immersed in cold or hot water maintained at noxious (4–8\textdegree C) or non-noxious (10 and 42\textdegree C) temperature, until the tail will be withdrawn. The duration of immersion will be recorded and a cut-off time of 15 s will be used.\textsuperscript{7}

Hot Plate test: Rats will be placed on the surface of hot plate maintained at a temperature of 55\textdegree C. The latency of the paw withdrawal will be noted down.\textsuperscript{14}

RESULT AND DISCUSSION

Acryllamide is a potent chemical entity which destroys the axons in the peripheral nerves, leading to irreversible neuropathy in the animals. Acrylamide (ACR) is a water-soluble, vinyl monomer that has multiple chemical and industrial applications: e.g., waste water management, ore processing. In addition, ACR is used extensively in molecular laboratories for gel chromatography and is present in certain foods that have been prepared at very high temperatures. ACR is well documented neurotoxicant in both humans and laboratory animals. Subchronic, low-level occupational exposure of humans to ACR produces neurotoxicity characterized by ataxia, skeletal muscle weakness and numbness of the hands and feet repeated daily exposure of laboratory animals (rodents, rabbits, dogs, cats and Guinea pigs) to ACR (0.5–50 mg/kg per day) is associated with neurological signs that, in many respects, resemble the neurotoxicity occurring in humans; i.e., ataxia and skeletal muscle weakness ACR intoxication at 10–50 mg/kg per day produces a triad of neurological deficits; i.e., hindlimb foot splay, ataxia (open field gait abnormalities) and skeletal muscle weakness (decreased fore- and hindlimb grip strength. Experimental ACR intoxication was also associated with neurogenic autonomic dysfunction; e.g., urinary retention, baroreceptor dysfunction, impaired vasomotor control.

In the present investigation, it is evident that \textit{Cassia fistula} was unable to protect the peripheral neuropathy in the animals. At all the therapeutically active doses the CHFA was unable to inhibit the peripheral motor neuro inflammation. It could be deduced that the axonal damage by acryllamide couldn’t be reversed by the CHFA. The reason could be the severe neurotoxic nature of acryllamide in comparison to the other neurotoxic agents or other surgical methods used by various researchers. There are remarkable areal differences in the vulnerability of the nervous system to ethanol-induced degeneration. Studies have shown an ethanol-induced loss of neurons, for example in the hippocampus frontal association cortex and in the cerebellum whereas in some areas, as in the motor cortex the number of neurons does not seem to be reduced. Ethanol-induced alterations in the autonomic nervous system have also been reported. Both acute and chronic ethanol intake increase plasma catecholamine concentration and chronic intake may cause a dysfunction of the autonomic nervous system, which is seen as impaired baroreceptor function, poor thermoregulation, and disorders of gastrointestinal motility. It has been reported previously that neuronal vacillation, decreased neuronal packing density, and increased lipo pigmentation in the cervical sympathetic ganglia after long-term heavy ethanol exposure.

In the present investigation, the rats were exposed to alcohol and the mono neuropathy that was developed in the vehicle treated group was reversed by the treatment with CHFA in dose dependent manner. This therapeutic activity could be attributed to the analgesic and anti oxidant property of the drug as reported by other authors. The results suggest that \textit{Cassia fistula} could be of immense importance in the amelioration of the mono neuropathy in the human beings. The hydro alcoholic extract should be further fractionated and tested against other models of neuropathy in the animals.

CONCLUSION

From present investigation, it is concluded that \textit{Cassia fistula} is unable to protect the animals from acrylamide induced peripheral neuropathy in dose dependent manner. As at all the therapeutically active
doses the CFHA was unable to inhibit the peripheral motor neuro inflammation. It could be deduced that the axonal damage by acrylamide couldn’t be reversed by the CFHA. While Cassia fistula is able to reverse the alcohol induced peripheral neuropathy in dose dependent manner in the animals.

REFERENCES
Fig 1: Graph showing results for motor activity (Rotarod)

Fig 2: Graph showing results for tail flicking latency
Fig 3: Graph showing results for paw withdrawl latency (Hot plate)

Fig 4: Graph showing results for motor activity (Rotarod)
Fig 5: Graph showing results for tail flicking latency

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