Advances in Bioresearch
Adv. Biores., Vol 16 (2) March 2025: 25-29
©2025 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.16.2.2529

Advances in Bioresearch

ORIGINAL ARTICLE

Evaluation of Cerebroprotective effect of *Actinidia deliciosa* fruit juice against Ischemia Occlusion/Reperfusion Injury in rats

Chakali Ayyanna [1]*, Muneendra. C [2], Shashidhar. K [3], Kalyan.M [4], Guruprasad .K [5], Eshwar Reddy.Y [6]
[1]. Associate Professor, Department of Pharmacology Creative Educational Society's College of Pharmacy, Chinnatekur, Kurnool,A.P- 518218
[2,3,4,5 & 6] .Creative Educational Society's, Department of Pharmacology, Chinnatekur, Kurnool, A.P- 518218
Corresponding author's Email: ayyannac5@gmail.com

ABSTRACT
Atinidia deliciosa has been used as natural origin medicine in the treatment of Cerebroprotective effect. This present study was designed to identify the possible role of Atinidia deliciosa fruit juice against ischemia-reperfusion induced oxidative stress modifications in the brain. Sprague Dawley (SD) rats (200–250 g) were induced to bilateral common carotid artery occlusion (BCCAO) for around 30 min later subjected to reperfusion for 24 h to induce cerebral injury by reperfusion. Atinidia deliciosa fruit juice (200 and 400 mg/kg, p.o) was administered continuously for 14 days and animals were subjected to ischemia-reperfusion injury. Different biochemical parameters were assessed subsequently. Fourteen days Atinidia deliciosa fruit juice (200 and 400 mg/kg, p.o.) treatment very significantly improved neurobehavioral alterations when compared to control ischemia-reperfusion. Atinidia deliciosa fruit juice (200 and 400 mg/kg, p.o.) treatment significantly attenuated oxidative damage when compared to ischemia-reperfusion (I/R) group animals. The data from this study recommend that treatment with Atinidia deliciosa fruit juice (200 and 400 mg/kg, p.o.) Increases the antioxidant protection against BCCAO-induced global cerebral ischemia and demonstrates cerebroprotective activity.
Keywords: *Atinidia deliciosa, Ischemia, Reperfusion, Neuroprotective, Cerebral ischemia*

Received 09.01.2025 Revised 21.01.2025 Accepted 05.02.2025

How to cite this article:
Chakali A, Muneendra. C , Shashidhar. K , Kalyan.M , Guruprasad .K , Eshwar Reddy.Y. Evaluation of Cerebroprotective effect of *Actinidia deliciosa* fruit juice against Ischemia Occlusion/Reperfusion Injury in rats. Adv. Biores. Vol 16 [2] March 2025. 25-29

INTRODUCTION

Brain tissue needs continuous supply of oxygen and glucose in order to maintain structural and functional integrity. It has been reported that the cerebral ischemia is the third leading causes for death in many developing countries behind other cerebrovascular disorders such as ischemic heart disease [1, 2] . Cerebral ischemia is a major factor and cause of mortality and morbidity followed by traumatic brain injury resulting from head injury [3-5]. Cerebral ischemia occurs when the blood flow to the brain is restricted, and it claims the lives of millions worldwide [3-5]. In total, 16% of humans will have a stroke during their life- time, with >15 million cases noted annually [6-7]. Stroke is a complex disease with a narrow time window for therapeutic intervention to restore the blood supply and prevent permanent brain tissue damage [8]. Ischemic occlusion generates thrombotic and embolic conditions in the brain [9].The mechanisms underlying the hypoxia harm include energy failure and loss of particle physiological state, excitotoxicity, loss of calcium physiological state, acidosis, cytokines and inflammation, changes in systems control protein synthesis, native microvascular reaction to ischemia-reperfusion (I/R), production of free radicals, alterations in genes expression and necrobiosis either apoptotic or death necrobiosis. The scientific name for the kiwi is Actinidia deliciosa [10]. It is also known as Chinese gooseberry, this fruit is popular all over the world, due to its high nutritional value, high content of vitamin C, in addition to excellent organoleptic qualities, in connection with its adaptability. Many researches [11-12] indicate that kiwi has more nutrients than other widely consumed fruits and emphasizes its therapeutic effects in terms of healthy metabolism, iron content, digestive potential,

antioxidant properties, immune function and also protective effects against coronary heart disease. . Kiwi fruit, as a source of ascorbic acid and polyphenols, helps reduce the risk of artery hardening, cardiovascular disease, and some types of cancer [13] in irritable bowel syndrome [14] and also protects cells in vitro oxidative damage to DNA. The present study was aimed to evaluate the cerebro-protective activity of *Actinidia delisiosa* against bilateral common carotid artery occlusion induced cerebral ischemia in Wistar albino rats.

MATERIAL AND METHODS

Collection of fruit:

The *Atinidia deliciosa*, were purchased from the local market of Kurnool. The fruit was authenticated by the botanist from Govt. Degree College for men, Kurnool.

Preparation of *Actinidia deliciosa* fruit *juice:*

The fresh fruit of *Actindia deliiousa* was prepared the help of juicer without addition of water. The fresh fruit was chopped into a small pieces and juice was collected. The juice was filtered with sterile cloth and the resultant filtrate was used and oral dosing to animal. fresh juice was subject The weight of petridish containing dry residue of juice was taken and equivalent dose of 50ml juice was calculated by subtraction initial weight of dried petridish. The same procedure was repeated for six times at different days. It was clear from the mean that, 50ml of juice gives 8.680mg f total solid residue in dried juice, which is equivalent to 143 gm of fresh juice of kiwi. The dose of fresh juice of kiwi (ml) equivalent to 200 and 400 mg/kg was administered orally to rats for 14 days [15]

EXPERIMENTAL ANIMALS:

30 Wistar rats weighing 220-260g were used in the present study. They were housed in individual polypropylene cages under standard laboratory conditions of light, temperature and relative humidity. Animals were provided standard rat pellets and drinking water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethical Committee of Creative Educational Society College of Pharmacy (IAEC/CESCOP/2023-03).

ACUTE TOXIITY STUDIES

Acute oral toxicity study in experimental rats was carried out as per OECD-423 guidelines. Four doses (5, 50, 300, 2000 mg/kg body weight) fruit juice of *Actindia deliciosa* were administered orally to groups containing three animals of the same age group and weight. The animals were regularly monitored for 1 hour continuously and then hourly for 4hr and finally after every 24hr up to 14 days for any symptoms of toxicity and mortality.

METHODOLOGY:

Induction of cerebral ischemia in rats

Ketamine (60 mg / kg,), xylazine (10mg / kg) was used to anesthetize rats. Both common carotid arteries were exposed between the sternocleidomastoid and the stern hyoid muscles parallel to the trachea through a midline incision and dissection on the ventral side of the neck. The common carotid arteries left and right were carefully separated and maintained from all muscles, ligaments, their adventitial sheath, and vagus nerve. Both common carotid arteries occluded 10 mins, 10 min reperfusion (1 cycle), cycle was continued to 3 cycles (MBCCAO/R). By using waxed silk suture, the skin was closed. Dilated pupils, absence of cornea reflex on light exposure and rectal temperature maintenance at 37 ± 0.50C observed after completion of 3 cycles. Hyperthermia development has been prevented using a heating lamp on the surgical table. [16]

Experimental design

S.no	Grouping	No. Of Animals (rats)	Treatment	Dose
1	I	6	Normal	Normal saline
2	II	6	Sham Control	Incision without O/R
3	III	6	Diseased Control	Occlusion/Reperfusion
4	IV	6	Low dose of *Actinidia deliciosa*	BCCAO/R+EEAD200mg/kg/P.O
5	V	6	High dose of *Actinidia deliciosa*	BCCAO/R+EEAD400mg/kg/P.O

After completion of 3 cycles rats were euthanized by C02 chamber and isolate the brain, subjected for estimation of cerebral infarction size and their homogenate used for estimation of glutathione , superoxidase dismutase (SOD) , and malondialdehyde (MDA) , and Catalase .

RESULTS AND DISCUSSION

Table No: 1 Percentage yield of ethanolic extract of *Actinidia deliciosa*

SL.NO	Name of the extract	Nature	Colour	Percentage yield (%)
1	Ethanolic extract of *Actinidia deliciosa*	Sticky	Reddish brown	5.2 %

Preliminary phytochemical analysis:

The ethanolic extract of *Actinidia deliciosa* was subjected to preliminary phytochemical analysis to assess the presence of various phytoconstituents. It revealed the following results

Table No:2 Preliminary phytochemical analysis of ethanolic extract of *Actinidia deliciosa*

Sl.No	Name of the test	Results
1	Alkaloids	+
2	Glycosides	+
3	Tannins	+
4	Flavonoids	+
5	Steroids	+
6	Terpenoids	-
7	Phenolics	+

+ Indicates present and – indicates absent

Acute toxicity study:

The fruit juice extract of *Actinidia deliciosa* was observed to safe up to 2000mg/kg by oral route. After 24 hours animals were found to be well tolerated. There was no mortality and signs of toxicity. Hence 1/5th (400mg/kg) and 1/10th(200mg/kg) of this dose were selected for biological study.

Table No: 3 Effect of *Actinidia deliciosa* on brain biochemical parameters in MBCCAO/R injury in rats

Treatment	Infarction size (%)	GSH (nmol/mg)	MDA (nmol/g)	Catalase (nmol/mg)	SOD (nmol/mg)	Dopamine (nmol/mg)
Normal rats	0	45.2±0.44	14.8±0.3	11.85±0.30	18.5±1.08	8.96±0.34
Sham rats	0	43.3±0.58	12.6±0.6	12.7±0.11	16.4±0.95	7.5±0.15
MBCCAO/R	100%	20.40±0.35###	29.5±0.45###	6.00±0.16###	9.48±0.95###	3.6±0.11###
Actinidia deliciosa 200mg/kg	47.75 %	29.55±0.39**	19.55±0.46**	7.70±0.37**	14.9±0.56**	6.5±0.22**
Actinidia deliciosa 400mg/kg	63.12%	41.72±0.45***	12.08±0.29***	9.71±0.14***	17.2±0.63***	8.13±0.08***

All values are expressed as mean ±SEM, n=6. Data were analyzed by one- way ANOVA followed by Dunnetts's test. ###p<0.001, **p<0.01, ***p<0.05, Normal vs MBBCAO/R, ###p<0.001, **p<0.01, ***p<0.05, Normal vs Sham control, ###p<0.001, **p<0.01, ***p<0.05, MBBCAO/Rvs Treatment groups. (i.e.: EE*AD* 200mg/Kg/P.O or EE*AD* 400mg/Kg/P.O)

DISCUSSION

Inadequate blood supply to an encephalon to fulfill metabolic demand is known as brain ischemia, also known as cerebral ischemia [17]. This condition is caused by the blockage of a major cerebral artery by an occlusion [18] or an embolism, which causes tissue destruction in the affected area and also deficiency of cerebral blood flow.

Oxidative stress is believed to be a major source for generation of post cerebral ischemic injury. Various experimental models of cerebral ischemic reperfusion injury showed significant neuroprotection when treated with antioxidants [19].

Lipid peroxidation has been established as a major mechanism of cerebral injury. The mechanism involves a process whereby unsaturated lipids are oxidized to form additional radical species as well as toxic by-products that can be harmful to the host system [20]. Polysaturated lipids are especially susceptible to this type of damage when in an oxidizing environment and they can react to form lipid

peroxides [21]. Lipid peroxides are themselves unstable and undergo additional decomposition to form a complex series of compounds including reactive carbonyl compounds [22].
Reactive species can be decreased or eliminated by a number of enzymatic and no enzymatic antioxidant mechanisms. SOD, which catalyzes the dismutation of the superoxide anion (O-2) into hydrogen peroxide and molecular oxygen, is one of the most important antioxidative enzymes [23]
In the present study, SOD and CAT activity decreased in the ischemic reperfused group compare to sham group and the results were in agreement with previous studies .This may be due to an excessive formation of superoxide anions. A decrease in SOD activity can result in the decreased removal of superoxide anions, which can be harmful to the brain. The decline in the enzyme level may be explained by the fact that excessive superoxide anions may inactivate SOD, thus, resulting in an inactivation of the H2O2 scavenging enzyme. The reduced SOD and CAT activity were increased by administration of the DL significantly when compared with the I/R group.
The reduction of GSH and elevation of MDA levels in the BCCAO group suggested enhanced lipid peroxidation and increased oxidative state in agreement with earlier reports [24]. Animals pretreated with EEAD 200 mg/kg and EEAD 400 mg/kg showed a reduction of lipid peroxidation as indicated by lower levels of MDA and increased GSH levels as shown in animals. Hence, this suggested that the mechanism of protection of the brain by EEAD 200 mg/kg and EEAD 400 mg/kg might be due to their antioxidant property. Glutathione (GSH) is one of the primary endogenous antioxidant defense systems in brain, which removes hydrogen peroxides, thus a decline in GSH levels in the BCCAO group could exacerbate the oxidative state [24]. It has been shown that depletion in GSH levels in ischemic reperfusion injury can be attributed to several factors such as cleavage of GSH levels to cysteine, decrease in synthesis of GSH and formation of mixed disulfides, causing their cellular stores to be depleted [24-25].
Superoxide dismutase is an important endogenous antioxidant which prevents production of free radicals as well as decomposing superoxide radicals to produce hydrogen peroxide whereas catalase decomposes the hydrogen peroxide and converts it to water and diatomic oxygen [26]. The reduction of SOD and CAT enzymatic activities by BCCAO compares well with the earlier reports [27], however, in the pretreated groups EEAD 200 mg/kg and EEAD 400 mg/kg the activities of both SOD and CAT were significantly higher compared with the BCCAO group, a reflection of the potency of the antioxidant capability. The increased production of SOD was matched by a subsequent elevation of CAT which therefore, prevented the accumulation of hydrogen peroxide, which on conversion to hydroxyl radicals might produce deleterious effect on the brain [28].
Brain MDA levels was significantly increased (29.5±0.45) in MBCCAO/R rats when compared with normal and Sham rat's respectively. while *Actinidia deliciosa* 200 mg / kg (19.55±0.46), *Actinidia deliciosa*(12.08±0.29), *Actinidia deliciosa* 400 mg / kg treated rats shows significantly decreased in MDA levels respectively.
Brain GSH levels was significantly decreased (20.40±0.35) in MBCCAO/R rats when compared with normal and Sham rats while *Actinidia deliciosa* 200 mg / kg (29.55±0.39), *Actinidia deliciosa* 400 mg / kg (41.72±0.45), *Actinidia deliciosa* 200 mg / kg treated rats shows significantly increased in GSH levels respectively.
Brain Catalase levels was significantly decreased (6.00±0.16) in MBCCAO/R rats when compared with normal and Sham rats while *Actinidia deliciosa* 200 mg / kg (7.70±0.37), *Actinidia deliciosa* 400 mg / kg (9.71±0.14), *Actinidia deliciosa* 400 mg / kg treated rats shows significantly increased in GSH levels
Percentages of Cerebral infract Size in *Actinidia deliciosa* (200mg/kg, 400mg/kg B.wt) treated rats the Percent Cerebral infract volumes were found to be reduced to 47.75 % and 63.12 % respectively. In this study there was a significant increase in percent cerebral infract in MBCCAO/R group compare to Normal and control group. Treatment with *Actinidia deliciosa* significantly reduced in percent cerebral infarct compare to MBCCAO/R group indicating the Cerebroprotective action of *Actinidia deliciosa*

CONCLUSSION

The results of present study concluded that ethanolic extract of *Actinidia deliciosa* (*EEAD*) possessed cerebroprotective activity against MBCCAO/R induced stroke rats. The data obtained from the study are consistent with the concept that ligating and reperfusion activity of the artery causes damage to rat's brain cells from MBCCAO/R play major role in inducing stroke. *EEAD* restored the levels of CAT, SOD, GSH LPO and neurotransmitters (Dopamine,) levels to normal. Hence, it can be concluded that 400 mg/kg shows significant cerebroprotective activity when compared to 200mg/kg may be due to the active constituent's present flavonoids in *EEAD*. Further studies are recommended to elucidate the mechanism of the cerebroprotective activity of *Actinidia deliciosa*.

REFERENCES

1. Dirnagl U., Iadecola C., Moskowitz MA.[1999]. Pathobiology of ischemic stroke: an integrated view. Trends Neurosci.,22(9):391-97.
2. Terent A., Marke L A., Asplund K., Norrving B., Jonsson E.[1994].Costs of stroke in Sweden. A national perspective Stroke.Stroke .,25(12):2363-69.
3. Wolfe C D., [2000].The impact of stroke. Dr Med Dull., 56(2):275-286.
4. Baethmann A., Eriskat J., Stoffel M., Chapuis D., Wirth A., Plesnila N.[1988]. Special aspects of severe head injury: recent developments. Curr Opin An aesth esiol., 11(2):193-200 .
5. Graham .D I., Adams .J H., Doyle D.[1978]. Ischemic brain damage in fatal nonmissile head injuries. J Neurol Sci.,39(2-3):213-34.
6. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, de Ferranti S, Després JP, Fullerton HJ, Howard VJ.[2015]. Heart disease and stroke statistics-2015 update: A report from the American Heart Association. Circulation 131(4): e29-322.
7. Di Carlo A.[2009]. Human and economic burden of stroke. Age Ageing., 38(1): 4-5.
8. Dong B., Yang Y., Zhang Z., Xie K., Su .L and Yu Y.[2019]. Hemopexin alleviates cognitive dysfunction after focal cerebral isch- emia-reperfusion injury in rats. BMC Anesthesiol., 19(1): 2-9.
9. Musuka .T D., Wilton .S B., Traboulsi M., Hill .M D.[2015]. Diagnosis and management of acute ischemic stroke: Speed is critical.CMAJ.,187(12):887–893.
10. Abhijeet Pandit Somawanshi ., Vijay Pawar.,[2022].The Review on Kiwi Fruit. IJRPR. 3(11):2392-2396.
11. Boeing H., Bechthold A., Bub A., Ellinger S., Haller D., Kroke A., Leschik-Bonnet E., Müller MJ., Oberritter H., Schulze M., Stehle P., Watzl B. [2012]. Critical review: vegetables and fruit in the prevention of chronic diseases. Eur J Nutr**.**, 51(6):637-63.
12. Chang WH., Liu JF.[2009]. Effects of kiwifruit consumption on serum lipid profiles and anti-oxidative status in hyperlipidemic subjects. Int J Food Sci Nutr., 60(8):709–713.
13. Puri DK., Manjula SN.[2018].Nutritional Content and Therapeutic Potential of Kiwifruit. World J Pharm Pharm Sci ., 7(6):536–565.
14. Chang CC., Lin YT., Lu YT,[2010]. Kiwifruit improves bowel function in patients with irritable bowel syndrome with constipation. Asia Pac J Clin Nutr.,19(4):451–457.
15. Upaganlawar A and Balarama.R.[2010]. Protective effects of *Lagenaria siceraria* fruit juice in isoproterenol induced myocardial infarction.IJP. 6(5):645-651.
16. Kumar A., Jaggi AS., Singh N.[2014]. Pharmacological investigations on possible role of Src kinases in neuroprotective mechanism of ischemic postconditioning in mice. Int J Neurosci.,124(10):777-86.
17. Ginsberg MD., Busto R.,[1989]. Rodent models of cerebral ischemia. Stroke., 20(12):1627–42.
18. McBean DE., Kelly PA.,[1998].Rodent models of global cerebral ischemia: a comparison of two-vessel occlusion and four-vessel occlusion. Gen Pharmacol.,30(4):431–4.
19. Thirumurugan G.[2010]. Behavioral assessment studies in cerebral ischemia induced by bilateral carotid artery occlusion in Rats. Ann Bio.,1 (1): 208-23.
20. Margaill I., Plotkine M., Lerouet D.[2005]. Antioxidant strategies in the treatment of stroke. Free Rad Biol Med., 39(4): 429.
21. Adibhatla.[2003]. Phospholipase A2, hydroxyl radicals, and lipid peroxidation in transient terebral ischemia. Antioxid Redox Signaling.,5(5): 647-54.
22. Kinuta Y., Kikuchi H., Ishikawa M., Kimura M., Itokawa Y.[1989]. Lipid peroxidation in focal cerebral ischemia. J Neurosurg.,71(3):421-29.
23. Akondi RB., Kumar P., Annapurna A., Pujari M.[2011]. Protective effect of rutin and naringin on sperm quality in streptozotocin (STZ) induced type 1 diabetic rats. IJPR., 10(3): 585-96.
24. Vekaria., R.H., Patel., M.N., Bhalodiya., P.N., Patel V., Desai T. R.' and Tirgar P.R. [2012]. Evaluation of neuroprotective effect of Coriandrum Sativum Linn. Against ischemic-reperfusion insult in brain.I J Phytopharmacol.,3(2):186-193.
25. Kosower N.S., and Seligman J.[1978]. Altered hepatic junctional permeability, bile acid, excretion and glutathione efflux during oxidant challenge. Pharmacology and Experimental therapeutics., 251:1069-75.
26. Govindarajan R., Vijayakumar M., Pushpangadan P. [2005]. Antioxidant approach to disease management and the role of 'Rasayana' herbs of Ayurveda. J Ethnopharmacol. ;99(2):165-78.
27. Chaudhary G., Sinha K., Gupta YK.[2003].Protective effect of exogenous administration of alpha-tocopherol in middle cerebral artery occlusion model of cerebral ischemia in rats. Fundam Clin Pharmacol.,17(6):703-7.
28. Pigeolet E., Corbisier P., Houbion A., Lambert D., Michiels C., Raes M, Zachary,, M-D and Remacle J.[1990].Glutathione peroxidase, superoxide dismutase, and catalase inactivation by peroxides and oxygen derived free radicals. Mech Age Dev.,51(3):283–297.