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Herbal Drugs Used in The Treatment of Stroke

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Abstract:

Stroke is one of the most important causes of mortality and morbidity in the world. Prevention and effective treatment of stroke is of the utmost importance. Cerebral ischemia causes disturbances in a variety of cellular and molecular mechanisms, including oxidative phosphorylation, membrane function, neurotransmitter release, and free radical generation. It has been years since tissue-type plasminogen activator (t-PA) became the first medication approved by the FDA for the management of stroke, with limited success. Thrombolytic therapy is the most effective therapeutic strategy for the prevention of brain injury and reduction of mortality in patients with cerebral infarction. However, a combination of established thrombolytic therapy and effective neuronal protection therapy may have more beneficial effects for patients with cerebral infarction. Because clinical trials of pharmacological neuroprotective strategies in stroke have been disappointing, attention has turned towards approaches which include herbal drugs that can be used in limiting the neurological damage associated with stroke. Herbal drugs may be used as prophylactic treatment in patients with high risk of stroke. Herbals drugs have been described in ancient systems of medicine for the treatment of various ailments associated with stroke and have more recently been reported to be beneficial in treating stroke. However, the strength of evidence to support the use of these herbal drugs is unclear. This review focuses on putative mechanisms underlying the beneficial effects of herbal drugs in patients with stroke and on the possibility of herbal drugs to increase the therapeutic time window in patients with cerebral ischemia.

Keywords: cerebral ischemia, neutroprotective, herbal drugs,thrombolytic therapy.

INTRODUCTION :

Stroke

A stroke is the sudden onset of weakness, numbness, paralysis, slurred speech, aphasia, problems with vision and other manifestations of a sudden interruption of blood flow to a particular area of the brain. The ischemic area involved determines the type of focal deficit that is seen in the patient.[1,2]

Transient Ischemic Attack (TIA)

A TIA is similar to a stroke, but the interruption of blood flow is temporary. The clot resolves sporadically. The symptoms are relatively the same as a stroke but last less than 24 hours, whereas stroke symptoms persist for greater than 24 hours.[17]

Causes of Stroke[1,2,3]

The primary pathophysiology of stoke is an underlying heart or blood vessel disease. The secondary manifestations in the brain are the result of one or more of these underlying diseases or risk factors. The primary pathologies include hypertension, atherosclerosis leading to coronary artery disease, dyslipidaemia, heart disease, and hyperlipidaemia. The two types of stroke that result from these disease states are ischemic and haemorrhagic strokes.

Non-reducible Risk Factors

The possibilities of a stroke occurring increases with age. For every decade (10 years) over the age of 55, the possibility of a stroke occurring doubles. A patient that is 75 years of age has four times the risk of having a stroke compared to someone who is 55 years old. Of all strokes that occur in people, approximately 65% occur in those who are over the age of 65.Those who have had a stroke or TIA are more likely to have another stroke or transient ischemic attack. Approximately 60% of strokes occur in patients who have had a previous TIA.Strokes generally occur more often in males than females, until the age of 55; after age 55 the risk is the same for both men and women.The occurrence of stroke is higher in the African-American, Hispanic, and Asian-Pacific Islander population than in other ethnical backgrounds.Patients who have immediate family members (mother, father, or sibling) that have had a stroke or TIA are at greater risk for having a stroke or TIA than those who do not have a family history with these events.People who have diabetes are also at greater risk of stroke that those without diabetes.

Reducible Risk Factors

Lower your high blood pressure. Hypertension (high blood pressure) is the number one most treatable risk factor for stroke. You can help prevent a TIA or stroke considerably by working to lower your blood pressure.Lowering cholesterol levels may decrease the risk of stroke. By working to lower your cholesterol, you can help prevent a TIA or stroke.Stop smoking. If you stop smoking, you can decrease your risk for stroke to that of a non-smoker within two to five year.

Common Symptoms

These symptoms usually occur suddenly without warning. Most patients are going about their normal daily activities and suddenly notice:

- ✓ A weakness or numbness in the face, arm, or leg.
- ✓ A change in the vision of one or both eyes that occur suddenly with no known cause.
- ✓ A severe sudden headache that cannot be explained by any injury or other cause.
- ✓ A quick onset of dizziness, loss of coordination/balance, or other problems walking.
- ✓ A sudden problem talking or expressing thoughts and words.

These are the most common signs and symptoms to be aware of and reasons to seek immediate medical attention. The symptoms most often affect only one side of the body but may affect both sides. If you see someone or you have any of these or other symptoms seek immediate medical attention – do not "wait to see if it goes away."

Other Symptoms

A sudden loss of consciousness or moments of fainting or convulsions (seizures) without any known cause. Nausea, vomiting, or fever that occurs suddenly (within minutes or hours) that cannot be explained by any other causebetes may also help to decrease your risk of stroke.

Treatment[1,2]

Thrombolytic Therapy

Thrombolytic therapy is the use of drugs to break up the clot that is causing the disruption in blood flow to the brain.It is imperative that you immediately go to the hospital when you first notice the warning signs of a stroke. The length of time between the first warning signs and the time you get to a hospital may directly affect your recovery. Patients who present to the hospital within 3 hours of the first sign of a stroke have the possibility to receive alteplase (Activase®). Activase® is a clot-buster. It breaks-up the clot to restore blood flow to the area of the stroke.There are many factors that determine whether or not a patient is able to receive thrombolytic therapy. One of these factors is the amount of time between the onset of symptoms and presentation to the hospital. If you get to the hospital within the 3 hour time frame and the doctor determines you are able to receive this clot-buster, you may have a better recovery.

Antiplatelet Agents – Mild Blood Thinners

Platelets are blood cells that are help the blood clot (stick together) and prevent bleeding. When the body has a cut, scratch, bruise, or bleed, platelets go into action and begin to work. They can be thought of as materials (like bricks or blocks) that aggregate (link together/ stack up) to form this clot. These platelet cells need thromoxane A2, adenosine, vitamin K specific clotting factors (chemicals produced by the body) to make them aggregate (stick) together. These chemicals can be thought of as the glue that holds the blocks together to make the clot. However, in patients who have had a TIA or stroke, the blocks don't need to stick together as much because this causes the blood to be too thick (like adding flour to milk when making a cake batter it makes it thicker and harder to stir or pour) and possibly form a clot that can't fit through the vessels.So, doctors often place stroke/TIA patients on blood thinners to decrease the possibility of the body forming another clot in the blood, which may lead to another TIA or stroke.

Aspirin

Aspirin is used for prophylaxis of TIA and/or stroke except in patients with an allergy to aspirin or salicylates.The mechanism of action for aspirin's stroke prevention is the inhibition of prostaglandin synthesis action to prevent the formation of platelet-aggregating substance thromboxane A2.The usual dose for this indication in adults is 50 – 325mg/day. Aspirin should be taken with food, milk, or large glass of water to decrease GI problems. Monitor for signs of bleeding.

Aspirin and Dipyridamole – Aggrenox®

Aggrenox® is used to reduce the risk of stroke in patients who have had a TIA or completed ischemic stroke due to thrombosis, except in patients with hypersensitivity to dipyridamole or aspirin.The mechanism for its antithrombotic action is the additive antiplatelet effect of the two drugs. The aspirin portion works the inhibition of prostaglandin synthesis action to prevent the formation of platelet-aggregating substance thromboxane A2, while the dipyridamole inhibits adenosine uptake into erythrocytes, endothelial cells, and platelets.

One capsule (aspirin 25mg and dipyridamole 200mg) twice a day is the usual dose in adults. The capsule should be swallowed whole (not chewed or crushed), and can be taken with or without food. Most patients experience a severe headache when initiating therapy due to the vasodilatation of dipyridamole. The headache should ease and resolve after the body adjusts to the treatment. In the meantime, acetaminophen (Tylenol) is the treatment of choice for the headache.

Clopidogrel – Plavix®

Clopidogrel is used to reduce future atherosclerotic events (stroke) in patients with a recent stroke.The drug's mechanism is it blocks the adenosine phosphate (ADP) receptors, which prevents fibrinogen binding to the receptor. This decreases the ability of platelet adhesion and aggregation.The usual dose for stroke prevention is 75mg once a day, and can be taken without food. It may be used as an alternative to aspirin containing products in patients allergic to aspirin or salicylates.

Clopidogrel and Aspirin

The combination of Clopidogrel and aspirin is used to reduce future atherosclerotic events (stroke) in patients with a recent stroke or patients who had a stroke while on Clopidogrel.The mechanism of action for each drug is different. Clopidogrel blocks the adenosine phosphate (ADP) receptors, which prevents fibrinogen binding to the receptor, while aspirin inhibits prostaglandin synthesis action to prevent the formation of platelet-aggregating substance thromboxane A2.The usual dose is clopidogrel 75mg tablet and an additional aspirin 325mg tablet a day. Patients may need to take the medications with food, milk, or a full glass of water to decrease GI problems. Do not dispense in aspirin/salicylate allergic patients.

Ticlopidine – Ticlid®

Ticlopidine is used in patients to decrease the risk of stroke or the occurrence of another stroke. However, due to its life-threatening rheumatologic disorders, it should be reserved for patient's refractory to aspirin or allergic to aspirin.The mechanism of action is unique among the antiplatelet drugs because it specifically

increases bleeding time.The usual dose is 250mg twice a day. It should be taken with food to decrease stomach upset.Starting the second week of therapy and through the third month of therapy, patients will need a complete blood count with differential every two weeks. The peak occurrence of thrombocytopenia (TTP) is 3-4 weeks after starting the medicine, with peak occurrences of neutropenia at 4-6 weeks, and aplastic anemia incidences after 4-8 weeks.

Oral Anticoagulant – Stronger Blood Thinners

Warfarin – Coumadin®

Warfarin is used for the treatment and prophylaxis of pulmonary embolism, venous thrombosis, and thromboembolic disorders, and to prevent recurrences of TIA's. In stroke patients, warfarin is most often used to prevent a cardiogenic embolism due to atrial fibrillation.The usual therapy for the prevention of a cardio embolic TIA or stroke in patient with atrial fibrillation is long term oral anticoagulation with a target international normalized ratio (INR) of 2.5 (range of 2.0-3.0)Warfarin's mechanism of action is interference with hepatic synthesis of vitamin K-dependent coagulation factors (II, VII, IX, and X). Foods high in vitamin K inhibit the effects of warfarin. Once patient is stabilized on warfarin, the patient should not change dietary habits. The patient needs to maintain a consistent amount of vitamin K (70-140mcg/day) in their diet. Foods that are high in vitamin K include: leafy green vegetables, pork and beef liver, and green teas. Patients should be instructed to avoid large amounts of alfalfa, broccoli, asparagus, Brussels sprouts, cauliflower, cabbage, kale, spinach, watercress, lettuce, and turnip greens, and to consult their pharmacist or doctor who monitors their warfarin therapy.Patients beginning warfarin will need to have weekly laboratory test done to evaluate and stabilize their therapy.

Prevalence

According to the World Health Organization, 15 million people suffer stroke worldwide each year. Of these, 5 million die and another 5 million are permanently disabled. High blood pressure contributes to more than 12.7 million strokes worldwide. In India 1.2 billion people suffering from stroke per year.Europe averages approximately 650,000 stroke deaths each year.In developed countries, the incidence of stroke is declining, largely due to efforts to lower blood pressure and reduce smoking. However, the overall rate of stroke remains high due to the aging of the population.

Social burden

A costly disease for individual, family and societal perspective.About half of stroke survivors have physical or cognitive impairment and therefore partial or complete dependency.Chronic disease, required long term therapy.

Benefits of Herbal medicine

A less side effects as compared to allopathic medicine. Safer used for longer period of time as compared to allopathic medicine.Excellent prospective for treatment of ischemic stroke. Permanent cure of disease, but in allopathic medicine disease is not cure permanently and provide only instant relief to the patient Natural

healing. Cost effective.More affordable and conventional medicine. Do not damage immune system but allopathic medicine may damage the immune system.

Rational

The allopathic drugs used for stroke treatment prevent or cure the stroke condition but it produces side effects. This chemical drugs leads to psychological dependence and adverse behavioural effects. Therefore, herbal drugs used over allopathic drugs because it shows very less side effects as compare to allopathic medication**.**

OBJECTIVE

➢ Related To search herbal medicines and classify them according to its effect on modifying stroke behaviour.

- Effect on against the depression.
- Effect on anxiety.
- Effect on High blood pressure.

➢ To identify the traditionally used herbal medicines in society which lacks any scientific claims.

HERBAL DRUGS FOR STROKE

1. Punarnava

Botanical Name: -Boerhaavia diffusa

Biological source: -Obtained from whole herb/root of Boerhavia diffusa linn belonging to family Nyctaginaceae

Chemical Constituents:-b-sitosterol, a-2-sitosterol, palmitic acid, ester of b-sitosterol, tetracosanoic, hexacosonoic, stearic, arachidic acid, urosilic acid, hentriacontane, b-Ecdysone, tricontanol etc.

Pharmacological use: - Immunomodulatory effects, Immunosuppressive activity, Hepatoprotective Activity, Analgesic and Anti-inflammatory activity, Antioxidant activity

Use in stroke: -It is nerve rejuvenator and it is given in case of sciatica or nervous weakness or even paralysis condition. [15]

Animal/human studies:- In 3-nitropropionic acid (NPA), sodium nitroprusside (SNP) induced oxidative stress in rat brain homogenates BDE treatment with dose significantly decreased the production of TBARS and increased the activities of antioxidant enzymes like catalase and superoxide dismutase along with increased concentration of non-enzymatic antioxidant, reduced glutathione (GSH). Similarly, BDE caused a

significant decrease in the lipid peroxidation (LPO) in the cerebral cortex. Inhibitory potential of BDE against deoxyribose degradation shows that BDE can protect hydroxyl radical induced DNA damage in the tissues. [18]

2. Bramhi

Botanical name: - Bacopa monnieri

Biological source: - It consist of fresh leaves & stem of the plant known as Bacopa moniera Linn. Family: Scrophulariaceae

Chemical constituents: -The best characterized compounds in Bacopa monnieri are dammarane-type triterpenoid saponins known as bacosides, with jujubogenin or pseudo-jujubogenin moieties as aglycone units. Bacosides comprise a family of knownanalogues. Other saponins called bacopasides I–XII have been identified more recently. The alkaloids brahmine, nicotine, and herpestine have been catalogued, along with D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacin and plantainoside B.

Pharmacological uses: -It was used as a brain tonic to enhance memory development, learning and to provide relief to patients with anxiety.

Use in Stroke: - Brahmi," has been used in the Ayurvedic system of medicine for centuries. Traditionally, it was used as a brain tonic to enhance memory development, learning and to provide relief to patients with anxiety or epileptic disorders.The bacosides aid in repair of damaged neurons by enhancing kinase activity, neuronal synthesis, and restoration of synaptic activity, and ultimately nerve impulse transmission.[16]

Animal/human studies:- Bacopaside I treatment produced significant reduction in neurological deficits at 22 and 70 h, and significantly reduced cerebral infarct volume and edema at 70 h, when compared with the ischemia group. Animal, that were orally treated with bacopaside I showed increased the brain ATP content, energy charge (EC), total adenine nucleotides (TAN), nitric oxide (NO) level, Na+K+ATPase and Ca2+Mg2+ATPase activity. Bacopaside I treatment also improved antioxidant enzyme activities including brain superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px), in varying degrees, compared with the ischemia group. In addition, three doses of bacopaside I markedly inhibited the increase in MDA content of the brain.[19]

3. Jatamansi

Botanical name: - Nardostachys Jatamansi

Biological source: -It consists of dried rhizome, stolons and roots of Valeriana wallichii belonging to family Caprifoliaceae.

Chemical constituents:- Alpha-patchoulenese, angelicin, beta-eudesemol, beta-patchoulenese, betasitosterol, calarene, calarenol, elemol, jatamansin, jatamansinol, jatamansone, n-hexacosane, n-hexacosanol, n-hexacosanyl arachidate, n-hexacosanyl isolverate, nardol, nardostechone, norsechelanone, oroselol, patchouli alcohol, seychelane, seychellene, valeranal, valeranone.

Pharmacological uses: -Hepatoprotective activity, Antidepressant activity, Anticonvulsant activity, Antioxidant and stress relieving activity.

Use in stroke: - Alcoholic and N-hexane extract of jatamansi prevent the lipid peroxidation and it is beneficial in stroke as it suppress oxicalosive stress. [(4)]

Animal/human studies: - The anti-stress effect of hydro-ethanolic extract of N. jatamansi was evaluated in reference to its antioxidant property. Wistar rats were divided into four groups naïve, stressed, T-200 and T-500 stressed with oral pre-treatment of N. jatamansi extract, Restraint of rats on metallic chambers for 4 h at 4°C was followed by sacrifice and assessment of stress-induced alterations in biochemical parameters, incidence and severity of ulcers. The In-vitro antioxidant activity of N. jatamansi was studied by measuring the free radical scavenging activity. N. jatamansi showed potent antioxidant activity and significantly reversed the stress-induced elevation of LPO and NO levels and decrease in catalase activity in the brain. The N. jatamansi possesses significant anti-stress activity, which may be due to its antioxidant activity. [(20)]

4. Garlic

Botanical name: -Allium Sativum

Biological source: -Lehsun consists of the fresh compound bulb of Allium sativum Linn belonging to family Liliaceae.

Chemical constituents: -Alliin,asulphurcontainingamino acid.Allicin- allyl sulphide.Polysulphide responsible for the unpleasant smell of the oil .Amino acid: Leucine, methionine, S-methyl cysteine, S-allyl cysteine. Allyl propyl disulphide. Vitamins: A, B, C and D. Fatty acid, mucilage and albumin.

Use in stroke: - Neuroprotective effect of garlic associated with control of free radical brust induced by reperfusion preservation of antioxidant enzyme, diallyldisulphate an active principal of garlic. [4,5]

Animal/human studies: - Reviewed human trials which were conducted since 1993. Only those trails which were conducted for a minimum period of two weeks and that addressed the following parameters had been included: (a) cholesterol- lowering effects, (b) inhibition of platelet aggregation (c) lowering of blood pressure and (d) other cardioprotective properties. They reported that since 1993, 44% of the clinical trials have indicated a reduction in total cholesterol and all the seven clinical trials on the inhibition of platelet aggregation showed positive response in both healthy subjects and subjects with CVD.[21]

5. Turmeric

Botanical name: -Curcuma longa

Biological source: -Turmeric consists of the dried rhizomes of curcuma longa belonging to family Zingiberaceae

Chemical constituents: - Turmeric include diarylheptanoids, a class including numerous curcuminoids, such as curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Curcumin constitutes up to 3.14% of assayed commercial samples of turmeric powder (the average was 1.51%); curry powder contains much less (an average of 0.29%). essential oils are present in turmeric, among which turmerone, germacrone, atlantone, and zingiberene are major constituents.

Use in stroke: - Curcumin possess multiple pharmacological properties (anti-inflammatory, anti-thrombotic, and anti-oxidative) and these properties further add on to its anti-ischemic property. The anti-ischemic effect of curcumin is believed to be contributed by its free radical scavenging activity which is unique upon having phenolic and diketonic groups present in its structure. The neuroprotective effect of curcumin is well documented over different neurotoxicants. These protective effects not only rescue the metabolite alterations but also improve brain edema, Evans Blue leakage and infarct size during ischemic brain injury (stroke).[4-5]

Animal/human studies: -pre-treatment with curcumin or 30 minute post-treatment significantly reduced brain water content and improved neurological outcome following a moderate controlled cortical impact in mice. The protective effect of curcumin was associated with a significant attenuation in the acute pericontusional expression of interleukin-1β, a pro-inflammatory cytokine, after injury. [22]

6. Ashwagandha

Botanical Name: - Withania somnifera

Biological source: - Itconsist of dried roots and stem bases of Withania somnifera Dunal, belonging to family solanaceae

Chemical constituents: - The plant contain the alkaloid withanine as the main constituent and somniferine, pseudowithanine, tropin and pseudotropin, hygrin, isopellederine, anaferine, anahygrine, and steroid lactons. The leaves contain steroid lactone, commonly known as withanolides**.**

Use in stroke: - Inhibiting pathological manifestation of PAF, such as indusing calcium overload and secondary brain damage in penumbra.[4-6]

Animal/human studies: - It has been reported that in rats, the Ashwagandha extracts exert in vivo neuroprotection against stress, and is due to the antioxidant properties of its constituents. Inhibiting pathological manifestation of PAF, such as indusing calcium overload and secondary brain damage in penumbra. It is used as antianxity and stress, and fight against depression.[4-6]

7. Sarpgandha:

Botanical name: - Rauwolfia serpentine

Biological source: - Rauwolfia consist of dried roots and rhizomes of Rauwolfia serpentina Benth belonging to family Apocynaceae.

Chemical constituents: - fauwolfia serpentina contains dozens of alkaloid of the indole alkaloid family including ajmaline, ajmalicine, reserpine, and serpentine, among others.

Use in stroke: - Used as antioxidant in stroke. Rauwolfia serpentina may have a promising role as a prophylactic drug in stroke induced experimental dementia due to its neuroprotective effect.[7-8]

Animal/human studies: - Methanolic root extract of Rauwolfia serpentina (RS) was studied against global cerebral ischemia induced dementia by occluding both common carotid arteries. RS were administered for 14 days before and 7 days after both common carotid arteries occlusion (BCCAO) and were continued during behavioral testing i.e. Morris water maze test and elevated plus maze test. At the end of allexperiment mice brain were removed and TBARS level, SOD level and infract size were determined.[23]

8. Talimkhana

Botanical name: - Hygrophilia ariculata

Biological source: -it is obtained from the seeds of plant of Hygrophilia ariculata belonging to family Acanthaceae.

Chemical constituents: - The plant contains 2-furancarboxaldehyde, 5-(hydroxymethyl), oleic acid, elaidic acid, isopropylester, 5-(hydroxymethyl)-2 (dimethoxymethyl) furan, methyl 2,6-difluorobenzoate.

Use in stroke: - It is Neuroprotective and antioxidant. Hygrophila auriculata show a neuroprotective effect in tGCI induced oxidative stress by protecting brain cells from reactive oxygen species scavenging and increase the endogenous antioxidant capacity of the brain to com-bat ISH/RF induced oxidative stress. Effect might explain apparent usage of this plant in the folklore claim for stroke. [9]

Animal/human studies: - The present study evaluated the in vivo antioxidant and neuroprotective effect of terpenoid rich fraction (TF) from Hygrophila auriculata in a rat model of transient global cerebral ischemia (tGCI). Materials and methods: Male Wistar rats were grouped as sham control, tGCI control, vitamin E and TF treated groups. Following 7 days of drug administration, animals were subjected to tGCI by permanent occlusion of both vertebral and transient occlusion of carotid arteries for 10 min followed by reperfusion. The neuroprotective effect was assessed by tGCI induced neurological, sensory motor deficit in rats. Brain antioxidants such as superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA) were investigated.[24]

9. Tulsi


Botanical name: - Ocimum sanctum

Biological source: - Tulsi consists of the fresh and dried leaves of Ocimum species like Ocimum sanctum L. and Ocimum basilicum L belonging to family lamiaceae**.**

Chemical constituents: - Fresh leaves and stem of Ocimum sanctum extract yielded somephenolic compounds (antioxidants) such as cirsilineol, circimaritin, isothymusin, apigenin and rosameric acid, and appreciable quantitiesof eugeno. The leaves of Ocimum sanctum contain 0.7% volatile oilcomprising about 71% eugenol and 20% methyl eugenol. The oil alsocontains carvacrol and sesquiterpine hydrocarbon caryophyllene. Two flavonoids orientin and andvicenin from aqueous leaf extract of Ocimum sanctum have been isolated.

Use in stroke: - Tulsi helps to protect and detoxify the body's cells and organs, it can also help reduce toxic stress by relaxing and calming the mind and offering many psychological benefits including anti-depressant activity and positive effects on memory and cognitive function.The psychotherapeutic properties of tulsi have been explored in various animal experiments that reveal that tulsi has anti-anxiety and anti-depressant properties, with effects comparable to diazepam and antidepressants drugs. Animal studies further reveal that tulsi enhances memory and cognitive function and protects against aging-induced memory deficits. Similarly, in human studies, tulsi has been observed to reduce stress.[(10)]

Animal/human studies: - A total of 60 albino rats of male sex were randomly selected. They were divided into five groups (per model) of six rats each. Control group received normal saline, standard group sodium valproate, and the test groups were given OS at three different doses. The anticonvulsant activity was screened using maximal electroshock seizure (MES) model and pentylenetetrazole (PTZ) model. Results were analyzed by ANOVA followed by post-hoc turkey's test.[(25)]

10. Chitrak

Botanical name: - Plumbago zeylanica

Biological source: - It consist of dried root part of Plumbago zellanica belonging to family Plumbaginaceae.

Chemical constituents: - Plumbagin, 3-chloroplumbagin, 3'-biplumbagin, Chitranone, zeylinone, isozeylinone, elliptinone, droserone, chitranone, zeylinone, isozeylinone, isoshinanolone, maritinone, 4-naphthoquinone, plumbagic acid, seselin, 5-methoxyseselin, suberosin, xanthyletin, xanthoxyletin**.**

Use in stroke: - It has Hypolipidimic and antiatherosclerotic activity. Active ingredient plumbagin have significant antioxidant abilities and may cure paralysis.[11]

Animal/human studies: - The neuroprotective activity of plumbagin against cerebral ischemia was investigated in another study. Plumbagin upregulated the expression of transcription factor Nrf2 in neuroblastoma cells. In vivo, administration of plumbagin significantly reduced brain damage and ameliorated the associated neurological deficits in a mouse model of focal ischemic stroke.[26]

11. Sendaw Mith:

Botanical name: - Halite

Biological source: - Halites occurs in sedimentary rocks of evaporate association, cave deposits and volcanic sublimates.

Chemical constituents: - Sodium chloride.

Use in stroke: - high intake of sodium was associated with a significantly increased risk of stroke.[12]

12. Malkangni

Botanical name: - Celastrus paniculatus

Biological source: - It consists of seeds and leaves of plant Celastrus paniculatus Wild. Family Celastraceae.

Chemical constituents: - A triterpene compound lupeol isolated from pet. Ether extract of leaves of Celastrus paniculata was screened for wound healing activity. Identification of a new sesquiterpene polyol

ester has been characterized as a new sesquiterpene polyol ester characterized as 1α,6β,8β-triacetoxy-9β -benzoyloxydihydro-β-agarofuran , along with the 3 known compds.1α,6β,8α-triacetoxy-9α-benzoyloxydihydro-β-agarofuran , angulatueoid C , and 1α,6β,8β,14-tetraacetoxy-9α-benzoyloxydihydro-β-agarofuran , was isolated from the CCl4-sol. fraction of Celastrus paniculatus methanolic seed extract.

Use in stroke: - Among the medicinal properties of Celastrus paniculatus few are following. Oil extracted from the seeds of Celastrus are taken as an tranquilizing effect, besides being a central muscle relaxant, antiemetic, antiulcer genic and adaptogen with memory enhancing properties . In Indian traditional system of medicine, celastrus is used as an appetizer, laxative , emetic, aphrodisiac, brain tonic and used for the treatment of cough, asthma, leprosy, paralysis, leucoderma, rheumatism, gout and headache. The bark is reported to have abortifacient activity. [12]

Animal/human studies: - The aqueous, methanolic, chloroform and petroleum ether extracts of seeds of CP were investigated for their effect on cognitive functions in rats. Only the aqueous seed extract showed an improvement in learning and memory in both the shuttle-box and step-through paradigms. The effect of aqueous seed extract was also evaluated on oxidative stress parameters and found to show antioxidant properties by decreasing the lipid peroxidation and augmenting endogenous antioxidant enzymes in brain. [27]

13. Sadabahar

Botanical name: - Catharanthus roseus

Biological source: - It is dried whole plant of Catharanthus roseus belonging to family Apocynaceae.

Chemical constituents: -Alkaloids are the most potentially active chemical constituents of Catharanthus roseus. More than 400 alkaloids are present in the plant, which are used as pharmaceuticals, agrochemicals, flavor and fragrance, ingredients, food additives and pesticides. Thealkaloids like actineo plastidemeric, Vinblastine, Vincristine, Vindesine, Vindeline Tabersonine etc. are mainly present in aerial parts whereas ajmalicine, vinceine, Rosindin is an anthocyanin pigment found in theflower of C. roseus.

Use in stroke: - Sadabahar used for "brain health" (increasing blood circulation in the brain, supporting brain metabolism, increasing mental productivity, preventing memory and concentration problems and feebleness, improving memory and thinking ability, and preventing early aging of brain cell.[13]

Animal/human studies: - The leaves extract of Catharanthus roseus was investigated for hypotensive and hypolipidemic effects in adrenaline-induced hypertensive rats (AIHR) and compared with those of Atenolol in a crossover design. The pharmacologically active components responsible for hypotensive activities were isolated from plant using bioassay guided purification approach and the structure of the compounds was proposed by spectroscopic methods Catharanthus roseus leaves extract and commercial drug Atenolol were administered through intraperitoneal (i.p) route for one week. Different biochemical parameters such as heart weight, blood glucose level, serum cholesterol level, serum triglyceride level, body weight and the relationships between them were measured.[28]

14. Anar

Botanical name: -Punica granatum

Biological source: -The pomegranate (*Punica granatum*) is a fruit-bearing deciduous shrub in the family Lythraceae.

Chemical constituents: - Icosanoic, Linolenic, Oleic, Palmitic-, Punicic, Stearic acid. Citric acid, Malic acid was the second most abundant. Phenolic compounds like gallic acid, protocatechuic acid, chlorogenic acid, caffeic acid, ferulic acid, o – and p -coumaric acids, catechin, phloridzin and quercetin.

Use in stroke: - Prevents blood clots in the heart and arteries, also urinary retention. The seeds prevent your blood platelets from coagulating and forming clots. [4]

Animal/human studies: - Antioxidant and neuroprotective actions of P. granatum, this study was designed to evaluate the effect of methanolic leaf extract of P. granatum on global induced brain injury in Wistar rats. The MePG has exhibited potent antioxidant activity. Further, the MePG has significantly inhibited the generation of nitrite, ROS and TNF-α in LPS-induced RAW 264.7 cell lines. Besides, global ischemia followed by reperfusion caused significant changes in the neurological and behavioral functions in control animals compared to sham control. [29]

15. Adrak

Botanical name: -Zingi officinale

Biological source: -It is obtained fromdried rhizome of *Zingiber officinale* belonging to family Zingiberaceae.

Chemical constituents: -An oil liquid comprising of homomlogous phenols called gingerol (cardiotonic compounds) accounts for the pungency as well as the pharmcological activity of ginger. Gingerols upon dehydration form shogaols and further degrade to zingerone.Apart from the gingerols ginger constitutes of 50-70% carbohydrates present as starch, 3-8% lipids which includes free fatty acids like linoleic, linolenic, palmitic, oleic, capric, lauric and myristic, triglycerides and lecithins. The resinous matter constitutes 5-8% and volatile oil around 1-2% of the constituents in ginger. The aroma of ginger is mainly due to oil of ginger which contains a mixture of over 50 constituents. Volatile oils consist mainly of the sesiquiterpenes (β-besabolene and zingiberene), monoterpenes (β-phelandrene, cineol, borneol, and citral) and the sesquiterpene alcohol zingiberol.

Use in stroke: -Ginger has antiplatelet aggregation property which is due to the inhibition of thromboxane synthesis. Ginger also lowers cholesterol levels by inhibition of cholesterol biosynthesis under the assumption of inhibiting HMGCoA reductase.[14-5]

Animal/human studies: - In human platelet-rich plasma, gingerol and indomethacin prevented the secondary aggregation and blocked ATP release from platelets induced by adenosine 5'-diphosphate and adrenaline but had no influence on the primary aggregation. The maximal antiplatelet effect was obtained when platelets were incubated with gingerol for 30 min and this inhibition was reversible. It is concluded that the antiplatelet action of gingerol is mainly due to the inhibition of thromboxane formation.[30]

16. Gotu kola

Botanical name: -Centella asiatica

Biological source: - Gotu kola, is an herbaceous, frost-tender perennial plant in the flowering plant family Apiaceae.

Chemical constituents: -The chemical constituents of Centella includepolyacetylenes, triterpenoids, asiaticosides. Asiatiocides are useful antileproic agents. The present studies undertaken on C. asiatica in view of its attributed medicinal significance haveresulted in the isolation and structure elucidation of three new compounds named as centellin, asiaticin and centellicin.

Use in stroke: -Protect against glutamate or beta-amyloid induced neurotoxicity, decrease blood brain barrier permeability and mitochondrial injury. (4-5)

Animal/human studies: - Colchicine was administered intracerebroventricularly in the lateral ventricle of male Wistar rats. Morris water maze and plus-maze performance tests were used to assess memory performance tasks. Various biochemical parameters such as lipid peroxidation, nitrite, reduced glutathione, glutathione-S-transferase, superoxide dismutase, acetyl cholinesterase were also assessed. ICV colchicine resulted marked memory impairment and oxidative damage. Chronic treatment with Centella asiatica extract for a period of 25 days, beginning 4 days prior to colchicine administration, significantly attenuated colchicine-induced memory impairment and oxidative damage. Besides, Centella asiatica significantly reversed colchicines administered increase in acetyl cholinesterase activity. Thus, present study indicates protective effect of Centella asiatica against colchicine-induced cognitive impairment and associated oxidative damage. (31)

17. Tobacco

Botanical name: - Nicotiana tobacum

Biological source: - The plant is part of the genus *Nicotiana* and of the Solanaceae family.

Chemical constituents: - The lipid constituents, free fatty acids, triglycerides, sterol esters and free sterols of 11 cultivars of tobacco from Argentina were investigated by gas-liquid chromatography. Palmitic, oleic and linoleic acids were the major components in all fractions studied. Sitosterol was the main component of the free sterol and sterol ester fractions. Oil and protein contents, as well as some physicochemical characteristics of the oils, are also reported.

Use in stroke: - Inhibit neural nitric oxide synthase, protect against neurodegeneration.(3)

Animal/human studies: - Nicotine evokes improvement in learning and memory mediated through NPYY1receptors in AD like condition induced by colchicines in rats. In this study the cognitive functions were assessed by Morris water maze task and on acute nicotinic administration, dose dependent improvement in learning and memory in colchicines treated rats was observed. Nicotine decreased escape latency and increased the time spent in target quadrant as compared to the saline treated rats. [32]

CONCLUSION: -

Herbal compounds have vast therapeutic potential and used as a treatment measure in stroke. The review provide a compilation of herbal plants which are used for the treatment of stroke. It also provides some plants which are used for the prevention of stroke and used for the treatment of common post-stroke symptoms. Because of availability, lower cost, and fewer adverse effects of herbal compounds in comparison to synthetic makes them as an excellent choice in treating stroke. Further studies on investigating mechanism of action anddrug development for the stroke from such herbs may help in the therapeutic management of this chronic, morbid and debilitating disease

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