



Herbal Medicine for Stroke

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Early humans marvelled at and worshipped Nature. It can only be surmised that some *shaman* or medicine-man discovered that wounds and injuries could be healed at least partially by some special leaves or some barks or some such things. Doubtless he would also utter an incantation or two over it. But he must have realized that the incantations could certainly impress onlookers, but they were not of much use without the *special herbs* only he knew about. The accidental discovery of the burial site of a cave in Northern Iraq, uncovered the fact that approximately 60,000 years back mankind knew of herbs that were somehow important. It is interesting to imagine that the grave was that of a *shaman* and those herbs were his *special* herbs which he might need in the next world.

Seven of those herbs are still used throughout the World (1). The Assyrians, the Chinese, the Egyptians, the Hindus, the Greeks, the Mayans, the Incas have all left records of substances they used as medicines. The earliest recorded materia medica was compiled at the command of King Assurbanipal (668-627 BC), who ruled at Nineveh in Sumeria (Northern Iraq). The Hindu savants, Charaka and others, taught the use of herbs to their students around 2,000 years back. The *Charaka Samhita* describes some 600 different herbs and their uses, and is the principal Ayurvedic book of internal medicine(2). The Chinese Materia Medica was compiled in the early years of the Christian Era and comprises some 6,000 entries (1). The Encyclopedia of Traditional Chinese Medicine Substances, contains 5,767 entries and is the most definitive compilation of China's herbal tradition to date

(1). Traditional Chinese medicine was brought to Japan via Korea.

Folk medicines of many countries have a very long tradition of herbal and mineral-based therapies. These have been introduced, empirically perhaps, over many years and have, seen much practice, those that were of not much use have certainly fallen in disuse. There is undoubtedly a lot of "mumbo-jumbo" in it, but a very large number have definite medicinal properties. They have been tried and tested many thousands of times over the centuries--modern medical practice tends to scoff at this tradition, but medicines like Digitalis, Cinchona, Willow bark(we know it as a progenitor of acetylsalicylic acid), Curare, Nux vomica (the source of strychnine), Ergot are still well-known. Till the end of World War II, a lot of respected National Pharmacopoeias of the Western World contained these crude drugs or their principal ingredients. After the explosion of chemical knowledge which followed World War II, we still have to pay homage to the alkaloids of Vinca, to Taxol (originally from the Yew tree), to Artemisia. Herbs still used as such in the U.S.A. are garlic (*Allium sativum*), *Gingko biloba*, Saw palmetto (*Serenoa repens*), and St. John's Wort (*Hypericum perforatum*). To these must now be added turmeric(*Curcuma longa*), a material under development, at the Central Drug Research Institute Lucknow India.(3)

About one-quarter of the prescription drugs dispensed by community pharmacies in the United States contain at least one active ingredient derived from plant material (4). The World Health Organization (WHO) estimates that 80 percent of

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the world population (4 billion people) use herbal medicine for primary health care (5) in developing countries.

The field of stroke has seen many failures, more than a hundred compound have been investigated for their neuroprotective effects but none has yet reached the market. It is clear that more novel treatments are needed to protect stroke-damaged neurons.

Plant-derived Products May Protect Neurons from Metabolic Stress Following Stroke

The recent development of natural drugs for stroke has been prioritized. In China ,stroke is treated using traditional chienesese medicine (TCM). More than 100 chienesese medicines have been used for stroke prevention and therapy. Various plants & plant derived products are under clinical evaluation for the management of stroke are:

Carotenoids a group of naturally occurring plant pigments that range in colour from yellow to red, are well recognized for their antioxidant properties. Epidemiological evidence has shown that consuption of carotenoids from fruits and vegetables is protective against chronic diseases. Individuals consuming the high quantities of dietary beta-carotene have been shown to have a lower risk of cardiovascular problems, stroke, and some cancers, while increased risk of these diseases has been found in individuals having low quantity of beta-carotene consuption or low plasma beta-carotene concentrations.

Phenolic substances, especially polyphenols are widely distributed in plants. Various chemical properties and biological effects of dietary polyphenols play important role in protection against cardiovascular risks. Antioxidant and anti-inflammatory properties of polyphenols are attributed to their flayonoid class of compounds Recent studies provide evidence that polyphenols from grapes ameliorate neuro-degenerative changes. Individual polyphenolic compound such as resveratrol and genistein protect neurons and astrocytes from oxidatative damage (6).An obvious

hypothesis is that the antioxidant properties of polyphenols might protect blood vessels against the deleterious consequences of oxidative problems/ stress associated with many if not all cardiovascular risk factors. The protective effect of dietary poyphenols against vascular risk i.e. their ability to decrease the ischaemic obstruction events rate might be attributed in part to their ability to retard the progression of early atherosclerotic lesions to advanced plaques which are prone to ruptute with superimposed thrombosis.

1. The only surviving species of the ancient plant group **Ginkophyta.- Ginkgo biloba** is native to China ,has survived through cultivation in temple gardens and is now grown worldwide in parks and gardens. *Ginkgo biloba* is one of Europe's most lucrative phytomedicine (7). In Europe, ginkgo is used mainly against symptoms of aging. It is believed to stimulate circulation and oxygen flow to the brain, which can improve problem solving capacity and memory. It was shown to increase the brain's tolerance for oxygen deficiency and to increase blood flow in patients with cerebrovascular disease. (8). No other known circulatory stimulant, natural or synthetic, has selectively increased blood flow to disease-damaged brain areas. In a French study, "the results confirmed the efficacy of ginkgo extracts in cerebral disorders due to aging" (9). In another experiment study, ginkgo showed consistent and significant improvement in the treated group, over the control group for various tests, including mobility, orientation, communication, mental alertness, recent memory, and other factors (10). A "digit copying test" and a computerized classification test confirmed the improved cognitive function related to use of this herb (11).

Ginkgo extracts stimulated circulation in the limbs, reduced coldness, numbness, and cramping. In elderly people, ginkgo intake improved the pain-free walking distance by 30 percent to 100 percent (12). It also lowered high cholesterol levels in 86 percent of cases tested and prevented oxygen deprivation of the heart (13). The ginkgo extract appears to affect neurons directly, as shown by a recent French study (14). Another French study

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proved protection against cell damage, by ultraviolet light (15).

A German study documented benefits of long-term ginkgo use in reducing cardiovascular risks, including those associated with coronary heart disease, hypertension, hypercholesterolemia, and diabetes mellitus (16). By maintaining blood flow to the retina, ginkgo extracts inhibited the vision deterioration in the elderly. An adequate amount of extract may reverse damage from lengthy oxygen deprivation of the retina. The assessment by doctors of the patients' general condition treatment with ginkgo showed a significant improvement. These results show that visual field damage from chronic lack of blood flow is reversible (17)

Ginkgo biloba is used both to prevent and treat stroke and, more important, it is nontoxic. Extracts of leaves are used medicinally to improve blood circulation in the brain, evidently aiding memory and concentration, and reducing the chances of a stroke. A substance in the leaves evidently inhibits Platelet Activating Factor, thus making the blood less sticky and less likely to produce clots. This herb has also been shown to inhibit free-radical formation. Ginkgo is widely used in Europe to treat complications of stroke, including memory and balance problems, vertigo and disturbed thought processes. Many studies show that this herb increases blood flow to the brain helps reduce fragility of the capillaries. In large amounts, ginkgo may cause diarrhea, irritability and restlessness.

2.Green Tea (*Camellia sinensis*) has a history of mythological proportions, no matter where in the world you look for. These days green tea is getting the majority of its press for its positive effects on health. This is due to the power of its constituents, which include carotenoids, chlorophyll, polysaccharides, fats, vitamin C & E, manganese, potassium and zinc. However experts agree polyphenols present in green tea provide most of the health benefits. These are polyphenols. Four of these polyphenols are of particular interest. Epicatechin (EG), epigallocatechin (EGC),

epicatechin gallate (ECG), and epigallocatechin gallate (EGCG). EGCG is a powerful antioxidant and has been found to be 20 times stronger than vitamin E in protecting brain lipids, which are very susceptible to oxidative stress (18). Green tea is a hypotensive, lowers blood pressure and increases blood flow to heart. Many heart attacks are brought on by blood platelet aggregation and green tea prevents the blood from clumping together and forming clots that can lead to stroke (19). One study indicates that 6000 Japanese women who were nondrinkers and nonsmokers, over age 40, who drank about five cups of green tea a day had a 50 percent decrease in the risk of stroke. Coffee can elevate cholesterol levels, whereas green tea helps to lower them. According to the pharmacological studies the polyphenolic compounds from green tea are able to prevent progression of atherosclerosis in animal models.

Prevention of Brain Damage. is because of the biological response of certain brain cells to an event such as stroke or brain injury. The normal DNA repair system may actually cause these cells to go into self-destruct mode. Researchers at the University of California, San Francisco (UCSF) believe that constituents found in green tea may block this system and prevent the release of cell-damaging oxygen radicals that lead to brain damage. The researchers studied the effects of two plant chemicals - gallotannin from green tea and nobotanin B from a plant called glory bush. Both were found to be 10 to 1,000 times more potent in blocking PARG activity than other blockers, and gallotannin was found to be 100 times more effective than antioxidants, chemicals that can soak up the toxic oxygen molecules.

3.Ginseng (*Panax ginseng*) is the common name of two species of the plant *Panax* (family Araliaceae). *Panax ginseng* is the Asian species and *Panax quinquefolius* is the American species. Ginseng has been extensively studied in China, Japan, and Korea and, to a lesser degree, in the United States. In its various forms, ginseng or its compounds have various physiological effects. These include antistress capabilities, antihypoxia effects (20), alteration of circadian rhythms by modifying

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neurotransmitters, (21) inhibition of platelet aggregation (22), alteration of plasma corticosterone (23), modulation of immune functions (22), and delay of the effects of aging (24).

Active ginsenosides significantly increased the survival of mice under acute hypoxia and protected the brain from ischemia and reperfusion injuries. The protective effect of ginsenosides in decreasing intracellular calcium has been attributed to increased ATPase activity. In addition, the ginsenosides significantly inhibited free-radical generation by xanthine-xanthine oxidase.

4. Garlic (*Allium sativum*) has been used in herbal medicine for thousand of years and it contains a number of active compounds for medicinal use. A large number of sulfur compounds from garlic have been identified, which include allicin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, trans-ajoene, cis-ajoene, dimethyl trisulfide, and vinyl dithiols. These sulfur-containing compounds are responsible for the beneficial effects of garlic intake. Pharmacological reports have indicated that garlic has protective activity against atherosclerosis, and more specifically stroke and myocardial infarction (25). Some investigations have shown that garlic prevents both the development and progression of atherosclerosis. Dietary garlic increases fibrinolytic activity. Garlic extracts can decrease the levels of low density lipoproteins. A recent report showed that atherosclerotic plaque volume can be reduced by the intake of garlic extracts for several years.

Garlic prevents ischemic stroke by 1) Lowering cholesterol levels; 2) Is a best anti-clotting herb, contains nine anticoagulant compounds; 3) Because of its blood-thinning effect it is a major herb for heart attack prevention, and 4) ability to help control high blood pressure. Studies show that taking garlic (raw or as a deodorized oil capsule) dramatically reduces platelet adhesiveness allowing improved circulatory function. In hemorrhagic stroke, garlic and its other anti-clotting herbal relatives increase further risk. (25)

Cat's Claw: (*Uncaria tomentosa*) (UT) commonly

known as cat's claw, since ancient times is being used to treat many diseases including asthma, arthritis, and other inflammatory diseases. In recent years studies have provided evidence supporting the anti-inflammatory and antioxidant properties of UT, even when given in very large amounts appear to have very low toxicity level which makes the herb very useful. Cat's claw is used in cancer patients for its immune stimulating effects, and prevention of stroke, and heart attacks and several other health related problems (26). Cat's claw has several groups of plant chemicals that are responsible for its actions and uses. Many alkaloids are isolated from UT. Out of the six main plant alkaloids isopteropodine, pteropodine, mitraphylline, isomitraphylline, ryncophylline, and isoryncophylline, three of these are proven to be effective immuno-stimulants. Ryncophylline has shown an ability to inhibit platelet aggregation and thrombosis in lab testing. This means this alkaloid may be useful in the prevention of stroke and reducing the risk of heart attack by lowering blood pressure, increasing circulation, and inhibiting both the formation of plaque on the arterial walls and formation of blood clots in the vessels of the brain, heart and arteries.

5. Ginger (*Zingiber officinale*). Ginger is a cardiac tonic, as it decreases cholesterol and improves poor circulation. Ginger reduces the clotting activity. (27)

6. Turmeric (*Cucurma longa*) Turmeric is an important herb in Ayurveda. Many studies have shown that the compound curcumin, present in turmeric, prevents the formation of blood clots. It is recently reported to prevent ischemic stroke (28).

Manganese complexes of curcumin and its derivatives were evaluated for radical scavenging and neuroprotective effects. The manganese complexes exhibited a great capacity to protect brain lipids against peroxidation. (28b)

7. Carrot (*Daucus carota*) in a Harvard study of 87,245 female nurses, the consumption of carrots (and to a lesser extent, spinach) significantly reduced stroke risk. Women who ate five servings of carrots a week suffered 68 percent fewer strokes

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than those who ate carrots less than twice a month. Carrots are rich in beta-carotene and other carotenoids, all members of the vitamin A family.

8. Spinach (*Spinacia oleracea*) Studies at Tufts University in Boston and the University of Alabama in Birmingham have demonstrated that folate has preventive effects for both heart disease and stroke. In the study, people who consumed little folate were compared with those who ingested the most. It was found that people who ingested the most were only half as likely to show narrowing of the carotid artery. (29)

9. English pea (*Pisum sativum*), Nearly all legumes contain genistein, a cancer-preventive nutrient. In addition to guarding against cancer, genistein also appears to have a significant anti-clotting effect. So, it may also help prevent ischemic stroke and heart attack. (30)

10. Willow (*Salix alba*) Willow bark is herbal aspirin, and a low-dose aspirin has been shown in several studies to reduce the risk of ischemic stroke by about 18 percent. (Low-dose aspirin also cuts heart attack risk by about 40 percent in men and 25 percent in women.) Willow bark and the other aspirin-like herbs are advocated for use to prevent and treat ischemic stroke. They are powerful anticoagulants. Hence, they may increase risk of hemorrhage, including hemorrhagic stroke. (31)

11. Bilberry (*Vaccinium myrtillus*) Compounds present in the *Vaccinium species* are reported to play several roles in human health maintenance. Effective inhibition of urinary tract infections and potent antioxidant properties of *Vaccinium* fruits have been documented. Bilberries, blueberries and huckleberries contain compounds known as anthocyanidins. European studies show that anthocyanidins prevent blood clots formation and also break down plaque deposits lining the arteries. Bilberries are also shown to help to maintain capillaries. These findings suggest that Bilberries might prevent ischemic stroke without increasing the risk of hemorrhagic stroke. (32)

Besides above mentioned plants there are reports from animal research on less identified

plants for antistroke activity.

Grape seed extracts showed neuroprotective effects on neuronal injury by inhibiting DNA damage in the gerbil hippocampus after transient fore brain ischaemia. (33) Ethanollic extracts of the fruits of *Alpinia oxyphylla* have a neuroprotective effect on glutamate induced neuronal apoptosis. Evening primrose oil is rich in gamma-linolenic acid (GLA), which has potent anti-clotting and blood pressure lowering actions. It is believed to be useful in the prevention of stroke and heart disease. (34)

Astragalus improves tissue oxygenation *Acorus calamus* helps restore brain tissue damaged by stroke. (35) Cayenne Pepper (*Capsium frutescens*) improves circulation and heart function without raising blood pressure. It also enhances the power of other herbs taken at the same time. Horsetail (*Equisetum arvense*) the silica in horsetail maintains the elastic connective tissue of the arteries. It promotes arterial impermeability to harmful lipids, preventing deposits. *Kava kava* helps to protect the brain against oxygen deprivation (36)

Pine-bark Grape-seed Extract and *Achillea millefolium* (Yarrow) in tea or tincture form, is effective for thrombotic conditions with hypertension, including cerebral and coronary thrombosis. Combining it with *Tilia platyphyllos* (lime blossom) is given in essential hypertension. (37). *Capsicum frutescens* (Cayenne pepper) is good for both types of stroke. This remarkable culinary herb is a classic, and powerful, "alterative" which means that it regulates an imbalance which has gone awry in either direction. In this case, if stroke is ischemic (due to a clot cutting off proper blood flow to the brain) the Cayenne will stimulate the return of blood to the cerebral tissues. If, on the other hand, stroke is hemorrhagic (a bleed inside the skull), the Cayenne will act as a local styptic (stanching blood flow).

Crataegus spp. (Hawthorne, white and black). This botanical is perhaps the most useful of the heart tonics, and works particularly well to strengthen connective tissue, which is needed post-

stroke for damage repair (38). *Trifolium pratense* (Red clover) is high in natural coumarin, a blood-thinning agent. Not to be used in hemorrhagic stroke. (39)

Acori graminei (AGR) rhizome and *Uncaria ramulus* (URE) have been widely used herbal medicines against ischaemia. In a study to evaluate the ischaemia induced neuronal death and cognitive impairments in rats AGR and URE significantly reduced ischaemia induced cell death. (40)

Alcoholic infusions of *Ptychopetalus olacoides* (PO) are used in traditional medicine by patients presenting age associated symptoms and those recovering from stroke. pharmacological studies on PO ethanolic extracts using hippocampal slices from wistar rats exposed to oxygen and glucose deprivation had significantly increased cellular viability and prevented the increase of free radicals content. (41) Spiramine-T a diterpene alkaloid isolated from *Spiracea*

japonica was shown to have neuroprotective effect on cerebral ischaemia-reperfusion injury (42). *Ocimum sanctum* (OS) a plant widely used in Ayurveda has been shown to possess anti-inflammatory, antioxidant, and cognition enhancing properties. In a pharmacological study. The methanolic extracts of OS significantly prevented hypoperfusion-induced functional and structural disturbances. (43)

These studies clearly warrant further investigations to examine structural specificity, target cellular sites and molecular mechanism of action of these botanical compounds. With the development of molecular biological techniques and the advances in genomics, the majority of drug discovery is currently based on the molecular approach. However, there is a widening gap between natural-product researchers in countries rich in biodiversity and drug discovery scientists immersed in proteomic and high-throughput screening.

12(6):350-355.

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