



A REVIEW ON *GRIFFONIA SIMPLICIFOLIA* – A NATURAL ANTI-DEPRESSANT

HD Mehta (Upadhye)*, SV Mangrulkar, AJ Chourasia

Priyadarshini J.L. College of pharmacy, Electronic Zone, M.I.D.C. Hingna road, Nagpur. 440016, India.

ABSTRACT

In our country, more than 2000 medicinal plants have been recognized. *Griffonia simplicifolia* Fabaceae Family, is an important medicinal plant for antidepressant. Because L-5-Hydroxytryptophan which is derived from seeds of *Griffonia simplicifolia* is an industrial source of a serotonin precursor. Its medicinal usage has been reported in the traditional systems of medicine. Serotonin is an important in regulating brain chemistry and is especially important in problems such as depression. Therefore, supplementing with *Griffonia* seed can raise serotonin levels and provide relief from depression and insomnia. The present review article discuss about *G. Simplicifolia*, its major active constituents, and its role in depression.

Key words: *Griffonia Simplicifolia*, Depression, Serotonin.

INTRODUCTION

The World Health Organization predicts depression will become the second-most burdensome disease in the next decade, with the greatest burden in North America and the United Kingdom (WHO, 2001). Currently, major depression accounts for 33.3% of patients in the United States, (Unutzer, 1987) and, at 160 million prescriptions annually, antidepressants are the most prescribed medication, despite the fact that recent meta-analyses show these as no better to treat mild to moderate depression (the major prescriptive reason) than placebo. (Fournier, 2010) Serotonin is an important in regulating brain chemistry and is especially important in problems such as depression. Clinical depression is due to impairment of central monoaminergic function, a deficiency in the neurotransmission mediated by serotonin (5-HT), 5-hydroxytryptamin, norepinephrine (NA) and dopamine (DA). The monoamine concentrations may be altered as a result of disrupted synthesis, storage or release or the concentrations may be normal but the postsynaptic receptors and / or sub-cellular messenger activity may be impaired Serotonin's cell bodies are located in brain raphe

and its axons project to frontal cortex where they may have important regulatory functions for mood, basal ganglia where limbic areas where they may modulate emotions, particularly anxiety. (Hindmarch, 2001; Gerard et al., 2006). Serotonergic projections also arrive in the hypothalamus where they can regulate eating, appetite, and weight as well as drive and pleasure and regulate the sleep-wake cycle. (Van et al., 1972)

Hence, it was clear that supplementing with *Griffonia* seed can raise serotonin levels and provide relief from depression and insomnia. (Wang, 2013) Because *Griffonia simplicifolia* is the largest source of the compound 5-HTP. Its seeds contain up to 20% 5-HTP, by weight. Studies that have been done on *Griffonia simplicifolia* suggest that when supplemented as an herb, it may rival the effects of supplementing 5-HTP in isolation. The lowest effect dose for rats is 25mg/kg of bodyweight, which is about 4mg/kg of *Griffonia simplicifolia* extract, assuming 20% 5-HTP content. This translates to following human doses; 275mg *Griffonia* (55mg of 5-HTP) for a 150 lb person, 350mg *Griffonia* (70mg of 5-HTP) for a 200 lb person 450mg *Griffonia* (90mg of 5-HTP) for a 250 lb person. It is unknown whether *Griffonia simplicifolia* has other bioactives other than 5-HTP. The human dosages listed above are derived from rodent studies, and are not optimal, which is why

Corresponding Author

HD Mehta (Upadhye)

Email: upadhyeheena@gmail.com

they are different from the optimal dose of 5-HTP. (Pathak, 2010)

Source

Griffonia simplicifolia is a woody climbing shrub native to West Africa and Central Africa. It grows to about 3 m, and bears greenish flowers followed by black pods. (Irvine, 1961) Botanical synonyms for the plant also include *Schotia simplicifolia* (Vahl ex DC) Baill.

Classification: (PORSPI 1992; LegumeWeb 2008)

Binomial name : *Griffonia simplicifolia* (DC.) Bail
 Synonyms : *Bandeiraea simplicifolia* (DC.) Benth.
 Kingdom : Plantae
 Division : Magnoliophyta
 Class : Magnoliopsida
 Order : Fabales
 Family : Fabaceae
 Subfamily : Caesalpinioideae
 Genus : *Griffonia*
 Species : *G. simplicifolia*
 Common Name : *Griffonia*
 Local name (Akan): Kajja, Atooto, Poopoo

GRIFFONIA SEED EXTRACT

Griffonia Seed Extract is a natural supplement which is taken from the extract of the *Griffonia simplicifolia* plant. The seeds of this plant are known to contain the herbal compound 5-Hydroxytryptophan (5-HTP). (Lemaire, 2002) This compound is also an important building block in the human body used to synthesize Serotonin. As one of the key neurotransmitters for controlling mood and sleep, increasing levels of Serotonin can alleviate anxiety, promote feelings of well-being. (Bosch, 2008) *Griffonia* Seed Extract is the most popular form of 5-HTP supplement sold today because it is herbally sourced and considered to be very safe.

CHEMICAL CONSTITUENT

The seeds of the plant are used as an herbal supplement for their 5-hydroxytryptophan (5-HTP) content. (Fournier, 2010) *G. simplicifolia* extracts have been evaluated as an oral spray, resulting in increased satiety in one study. (Lemaire, 2002) *Griffonia simplicifolia* also has a legume lectin called GS Isolectin B4, which binds to alpha-D-galactosyl residues of polysaccharides and glycoproteins. This supplement is often given by spider silk farmers to increase production of stronger silk. A new β -carboline alkaloid, griffonine (1), together with seven known alkaloids, hyrtioerectine B (2), 3-carboxy -6- hydroxyl - β - carboline (3), hyrtiosulawesine (4), 5-hydroxyindole-3-carbaldehyde (5), 5-hydroxy-3-(2-hydroxyethyl) indole (6), trigonelline (7), and 5-hydroxytryptamine (8) were isolated and

identified. Alkaloids 1, 2 and 4 showed growth inhibitory effects on the HepG2 cell line with IC50 values of 23.5, 9.6 and 19.3 $\mu\text{mol}\cdot\text{L}^{-1}$, respectively. (Wang *et al.*, 2013)

GRIFFONIA AND THE BRAIN

The 5-HTP which is active constituents obtained from *Griffonia simplicifolia* plants becomes a crucial player in the regulation of human mood. This is because the compound is the direct pre-cursor to serotonin, the neurotransmitter which generates pleasant mood states and the sense of mental calm. (Nolen, 1985) Serotonin cannot be directly supplemented by any other method, as it is not able to cross the blood brain barrier on its own. If serotonin is consumed as a dietary supplement, it would not end up reaching the receptors in the brain where it is needed to produce changes. However, 5-HTP does reach brain tissue and interacts directly with neurons. Once it enters the brain, it is converted into serotonin for immediate use. (Turner *et al.*, 2006)

PRODUCTION AND INTERNATIONAL TRADE

The seed of *Griffonia simplicifolia* is a serotonin precursor. Trade statistics are not available. In the early 1990s the annual export from Ghana to Germany amounted to 80 t. In view of the increased demand for 5-HTP in the Western world, the trade must have expanded since then. In 1999 the wholesale price of seed was US\$ 8–9 per kg. (Pathak, 2010)

MECHANISMS OF ACTION (Chadwick, 1975)

Griffonia simplicifolia contains 5-hydroxytryptophan is the precursor of serotonin. (5-hydroxytryptamine); boosts serotonin levels in CNS. 5-HTP acts primarily by increasing levels of serotonin within the central nervous system.

CLINICAL USES

DEPRESSION (Nicolodi, 1996)

The first large clinical trial using 5-HTP in depression was conducted by Sano in 1972. Using an open trial design, a total of 107 patients with endogenous unipolar or bipolar depression were given daily oral dosages of 5-HTP from 50 to 300 mg. Significant improvement was observed in 74 of the patients (69%), and no significant side effects were reported. The response rate in most of these patients was quite rapid (less than two weeks).

The issue of speed of response was subsequently addressed in a study of 59 patients with eight different types of depression. 5-HTP was administered orally in dosages from 150 to 300 mg daily for a period of three weeks. Thirteen patients (22%) were markedly improved, and another 27 patients (45.8%) showed moderate improvement. Of these 40 patients who improved, 20 (50%) began to show improvement within three days,

Studies in patients with either unipolar or bipolar depression have demonstrated significant clinical response in 2 to 4 weeks at doses of 50-300 mg three times a day, and 32 patients (80%) improved within two weeks of beginning treatment with 5-HTP. In a study employing positron-emission tomography (PET) scanning, eight healthy volunteers and six people diagnosed with major depression received infusions of radio labelled 5-HTP. The researchers found that significantly less 5-HTP crossed the blood-brain barrier into the brains of the depressed subjects than into the brains of the normal controls. A significant reduction in anxiety was observed on three different scales designed to measure anxiety.

In a study of 20 people with panic disorders, several experienced a feeling of "relief" after receiving 5-HTP. In contrast to many conventional antidepressants which may take 4 weeks or longer to achieve therapeutic response in most patients, those taking 5-HTP appear to have a significantly more rapid response. Japanese researchers administered 5-HTP to 24 patients hospitalized for depression. After two weeks of treatment, a "marked amelioration of depressive symptoms" was observed in seven patients diagnosed with unipolar depression. The administration of 5-HTP was also associated with a 30 percent increase in the levels of 5-hydroxyindolacetic acid, the primary metabolite of serotonin.

PHARMACOLOGICAL ACTIVITIES (Erick, 2006)

L-5-Hydroxytryptophan (5HTP) is decarboxylated "in vivo" to yield serotonin, a neuro-hormonal transmitter released by neurons in the brain, spinal cord and sympathetic ganglia. Its seed contains active drug 5-hydroxytryptophan (5-HTP). 5-HTP is an aromatic amino acid naturally produced by the body from the essential amino acid L-tryptophan. Produced commercially by extraction from the seeds of the African plant *Griffonia simplicifolia*.

THERAPEUTIC APPLICATIONS

L-5-Hydroxytryptophan is reported to be of greatest benefit in psychiatric and neurological disorders where there is a deficiency of neural serotonin. L-5-Hydroxytryptophan is cited as a natural relaxant, to help alleviate insomnia by inducing normal sleep, for the treatment of migraine and headaches and to aid in the control of cravings such as in eating disorders. (Wurtman, 1986) L-5-Hydroxytryptophan is also thought to assist and strengthen the immune system and may help to reduce the risk of artery and heart spasms. L-5-Hydroxytryptophan has also been cited in the management of Parkinson's disease (PD) and epilepsy.

SUMMARY AND CONCLUSION

According to literature survey it might be suggested that *Griffonia* seed raises serotonin levels in the brain. Some Researchers reveals little information regarding the toxicology of 5-HTP. A possible association with fatal eosinophilia-myalgia syndrome in the 1980s and 1990s has now been attributed to contaminated L-tryptophan. HPLC identification of the implicated contaminant tryptophan-4,5-dione (referred to in publications as "Peak X") has also been disputed in a review of the safety of 5-HTP, but remains a requirement of the US Food and Drug Administration for all commercial 5-HTP products. (Das, 2004) Rats fed 5-HTP for a year showed no toxicological effects, and no reports of human toxicity have been documented since the mid-1990s. (Kleeman, 2000; RTECS) Therefore Serotonin is important in regulating brain chemistry and is especially important in problems such as depression, insomnia, and eating disorders. (Halford et al., 2007) Theoretically, supplementing with *Griffonia* seed can raise serotonin levels and provide relief from depression and insomnia. Normally, Serotonin is made from tryptophan that is found in the foods that we eat. However, individuals suffering from anxiety, depression, insomnia and other mood disorders are often found to have low levels of Serotonin. While supplementing with tryptophan can be moderately effective, it is even better to use 5-HTP which is converted to Serotonin at a faster rate than tryptophan itself. 5-HTP is actually an intermediary in the production of Serotonin.

Griffonia is one of a small number of natural sources for 5-HTP which is why this supplement has become so popular. (Murray, 1998) *Griffonia* Seed Extract is metabolized within the liver where the active ingredient 5-Hydroxytryptophan can then enter the blood stream. Once it reaches the brain, it readily crosses the so-called Blood Brain Barrier to enter the nervous system. It is here that it can be converted into Serotonin and bind to receptors on the neurons. (Emanuele, 2010) It also has the opposite effect on Dopamine, another mood neurotransmitter in the brain. As levels of this chemical drop, it tends to potentiate the beneficial effects caused by Serotonin even more. Serotonin is sometimes called the "happiness" neurotransmitter, used to signal feelings of pleasure and contentment between neurons. (Van, 1980) Using *Griffonia* supplements will artificially increase levels of this neurotransmitter, producing a wide range of benefits for patient's mental state.

PROSPECTS

Griffonia simplicifolia will remain in high demand as a natural alternative for the antidepressant Prozac.

REFERENCES

- Acquaye D. Feasibility studies on economic and export potential of some selected Medicinal Plants in Ghana (Griffonia, Voacanga and Annatto). 1997.
- Bandeiraea simp licifolia -ILDIS LegumeWeb. www.ildis.org.http, //www.ildis.org/LegumeWeb?sciname=Bandeiraea+simp licifolia. Retrieved 2008-03-15.
- Bosch, C.H. Griffonia simplicifolia (Vahl ex DC.) Baill. In, Schmelzer, G.H. & Gurib -Fakim, A. (Editors). Prota 11(1), Medicinal plants/Plantes médicinales 1. [CD-Rom]. PROTA, Wageningen, Netherlands 2008.
- Calderon-Guzman D, Hernandez-Islas JL, Espitia-Vazquez I, Barragan-Mejia G, Hernandez-Garcia E, Santamaria-del Angel D, Juarez-Olguin H. Pyridoxine, regardless of serotonin levels, increases production of 5-hydroxytryptophan in rat brain. *Arch Med Res*, 35(4), 2004, 271-4.
- Chadwick D, Jenner P, Harris R. Manipulation of brain serotonin in the treatment of myoolonus. *Lancet*, 2, 1975, 434-435.
- Das YT, Bagchi M, Bagchi D, Preuss HG. Safety of 5-hydroxy-L-tryptophan. *Toxicol Lett*, 15, 150 (1), 2004, 111-22.
- Data from pharmaceutical substances Kleeman 4th ed.2000.
- Den Boer JA, Westenberg HG. Behavioral, neuroendocrine, and biochemical effects of 5-hydroxytryptophan administration in panic disorders. *Psychiatry Res*, 31, 1990, 267-278.
- Emanuele, E; Bertona, M; Minoretti, P; Geroldi, D. An open-label trial of L-5-hydroxytryptophan in subjects with romantic stress. *Neuro Endocrinology Letters*, 31 (5), 2010, 663-6.
- Erick H. Turner, Jennier M. Loftis, aaron D. Blackwell. Serotonin a la carte, Supplementation with the serotonin precursor 5-hydroxytryptophan. *Pharmacology and Therapeutics*, 109 (3), 2006, 325-338.
- Fournier JC, DeRubeis RJ, Hollon SD. Antidepressant Drug Effects and Depression Severity, A Patient-Level Meta-analysis. *JAMA*. 303(1), 2010, 47-53.
- Gerard J. Tortora and Sandra Reynolds Grabowski. Principles of Anatomy and Physiology. John Wiley & Sons, Inc, 10th edition, 2006.
- Halford JC, Harrold JA, Boyland EJ, Lawton CL, Blundell JE ,Serotonergic drugs , effects on appetite expression and use for the treatment of obesity. *Drugs*, 67(1), 2007, 27-55
- Hindmarch I. expanding the horizons of depression, beyond the monoamine hypothesis. *Psychopharmacol* 16, 2001, 203-218.
- IRVINE FR Woody Plants of Ghana. Oxford University Press, London, 1961, 308-309.
- Jamie E. Lamie E. Lamb, Satoaki Shibata, Irwin J. Goldstein, Purification and Characterization of *Griffonia simplicifolia* Leaf Lectins. *Plant Physiol*, 71, 1983, 879-887.
- Lemaire, Peter A, Adosraku, Reimmel K. An HPLC method for the direct assay of the serotonin precursor, 5-hydroxytryptophan, in seeds of *Griffonia simplicifolia*. *Phytochemical Analysis*, 13(6), (2002), 333-337.
- Mental health, New understanding, new hope. Geneva, Switzerland, WHO; 2001.
- Murray, N.D.M. 5-HTP-The natural way to overcome Depression, Obesity and Insomnia. Bantom Books, New York. 1998
- Nicolodi M, Sicuteri F. Fibromyalgia and migraine, two faces of the same mechanism. Serotonin as the common clue for pathogenesis and therapy. *Adv Exp Med Biol*, 398, 1996, 373-379.
- Nolen WA, van de Putte JJ, Dijken WA, Kamp JS. L-5HTP in depression resistant to re-uptake inhibitors. An open comparative study with tranlycypromine. *Br J Psychiatry*, 147, 1985, 16-22.
- Pathak Suresh Kumar , Tahilani Praveen, Jain, Nishiprakash And Banweer Jitendra, A Review On *Griffonia simplicifolia* – An Ideal Herbal Anti-Depressant, *International Journal of Pharmacy & Life Sciences*, 1(3), 2010, 174-181.
- PORSPI, Ghana Herbal Pharmacopoeia. Advance Press, Accra. Ghana. 1992.
- Registry of Toxic Effects of Chemical Substances (RTECS).
- Turner EH, Loftis JM, Blackwell AD, Serotonin a la carte, supplementation with the serotonin precursor 5-hydroxytryptophan. *Pharmacol Ther*, 109(3), 2006, 325-38.
- Unutzer J, Klap R, Sturm R, et al. Mental disorders and the use of the alternative medicine, results from a national survey. *Am J Psychiatry*, 157(11), 2000, 1851-1857.
- Van Hiele LJ. L-5-Hydroxytryptophan in depression, the first substitution therapy in psychiatry? The treatment of 99 out-patients with 'therapy-resistant' depressions. *Neuropsychobiology*, 6, 1980, 230-40.
- Van Praag HM, Korf J, Dols LC, Schut T. A pilot study of the predictive value of the probenecid test in application of 5-hydroxytryptophan as antidepressant. *Psychopharmacologia*, 25, 1972, 14-21.
- Van Praag HM, Lemus C. Monoamine precursors in the treatment of psychiatric disorders. *Pharmacology & Therapeutics*, 109(3), 2006, 325-338.
- Wang XZ, Wu FH, Qu W, Liang JY. A new β -carboline alkaloid from the seeds of *Griffonia simplicifolia*. *Chin J Nat Med*, 11(4), 2013, 401-5.
- Wurtman RJ, Wurtman JJ, eds. Nutrition and the brain. New York, Raven Press, 1986, 89-139.