WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 6, Issue 1, 304-310. Review Article ISSN 2277– 7105

ST. JOHN'S WORT: MINI REVIEW

Neha Sharma[1]*, Uma Advani[2], Monika Jain[3], Lokendra Sharma[4], Alka Bansal[5], Charu Jain[6]

[1,2]Senior Demonstrator, Department of Pharmacology, SMS Medical College, Jaipur, India.
[3]Pofessor and Head of the Department, SMS Medical College, Jaipur, India.
[4]Prof, Department of Pharmacology, SMS Medical College, Jaipur, India.
[5,6]Asst. Prof., Department of Pharmacology, SMS Medical College, Jaipur, India.

Article Received on
12 Nov. 2016,
Revised on 02 Dec. 2016,
Accepted on 23 Dec. 2016
DOI: 10.20959/wjpr20171-7613

***Corresponding Author**
Dr. Neha Sharma
Senior Demonstrator,
Department of Pharmacology,
SMS Medical College, Jaipur,
India.

ABSTRACT

St. John's wort (SJW) belongs to the Hypericaceae family. Its botanical name is *Hepericum perforatum Linn.* Its aerial part contain anthraquinone derivatives, hypericin, usigtoercin, protohypericin, phenolic acid and tannins. It inhibits the reuptake of monoamines, serotonin, dopamine and noradrenaline and the amino-acid neurotransmitters GABA and glutamate. The constituents of SJW are hypericin, pseudohypericin, flavonoids and oligomeric procyanidines, but the major constituent responsible for the antidepressant effect is thought to be hyperforin. St. John's wort (Hypericum perforatum) have been used in folk medicine for a long time for a range of indications including depressive disorders. It is under various phases of study for other conditions like for irritable bowel syndrome, social phobia, obsessive-compulsive disorder, generalized social anxiety disorder (GSAD), attention deficit hyperactive disorder (ADHD), in relieving fatigue in patients undergoing chemotherapy or hormone therapy for cancer. This herbal drug has fewer side effects than many conventional antidepressants and is better tolerated. SJW is a potent inducer of CYP3A4 which results in decreased efficacy of antiretrovirals, cyclosporine, tacrolimus, antiepileptics, irinotecan, and other chemotherapeutic agents.

KEYWORDS: St. John's Wort, antidepressant, hyperforin.

INTRODUCTION

St. John's wort (SJW) belongs to the Hypericaceae family. Its botanical name is *Hepericum perforatum Linn. Leaves of this* perennial herb are oblong with pale lower surface as shown

in figure-1.[16] Flowers in terminal corymbs blooms in the month of April and continue upto August.[1]

Figure-1: Plant OF H. Perforatum.[16]

It sporadically occurs in the damp forest of Himalaya in India and generally propagated by seeds. Its aerial part contain anthraquinone derivatives, hypericin, usigtoercin, protohypericin, phenolic acid and tannins. This herb possess sedative, antidepressant and astringent properties.[1] This herbal antidepressant is freely available in Germany and some other European countries.[2]

A lot of research work has been done on SJW but to ellaborate its newer uses that under various phases of clinical trial, this study was carried out. A systematic literature search was carried out using databases such as PubMed, Cochrane Reviews and Google Scholar to gather detailed information about SJW. Thirty seven trials were searched using these data bases for detailed study. This mini review is about the brief phytochemistry, newer uses and important drug interactions of SJW.

Mechanism of action of SJW

It was found that it inhibits the reuptake of monoamines, serotonin, dopamine and noradrenaline and the amino-acid neurotransmitters GABA and glutamate.[2]

The constituents of SJW are hypericin, pseudohypericin, flavonoids and oligomeric procyanidines, but the major constituent responsible for the antidepressant effect is thought to be hyperforin.[3][4] Hyperforin is excreted into breast milk at low levels. Low levels of hyperforin is reported to be excreted into breast milk.[5]

Uses of St john's wort

St. John's wort (Hypericum perforatum) have been used in folk medicine for a long time for a range of indications including depressive disorders.[6] Total 27 trials were considered in a previously done study, including 2291 patients who had "neurotic depression" or "mild to moderate severe depressive disorders." It was evident in the study that extracts of hypericum are more effective than placebo for the short-term treatment of mild to moderately severe depressive disorders.[6]

In another meta-analysis of 37 double-blind randomised controlled trials that compared clinical effects of *Hypericum* monopreparation with either placebo or a standard antidepressant in adults with depressive disorders, it was found that larger placebo-controlled trials restricted to patients with major depression showed only minor effects over placebo. But, marked effects were observed in older and smaller trials not restricted to patients with major depression.[7]

On the contrary, it was documented in systematic reviews published between 1996 and 2000 that such extracts are more effective than placebo and are comparable with older antidepressants in the treatment of mild to moderate depression.[8]

It is suggested that it may be as effective as imipramine or paroxetine, to treat mild to moderate depression.[9] While, some studies also have reported negative results.[10]

It has also been tried for the treatment of tobacco dependence. A randomized, blinded, placebo-controlled, three-arm, dose-ranging clinical trial was conducted by Sood A et al 2010, in which total 118 subjects received SJW(St. John's Wort) 300 mg, 600 mg, or a matching placebo tablet 3 times a day combined with a behavioral intervention for 12 weeks. They suggested that SJW has little role in the treatment of tobacco dependence.[11]

Previously it has been reported that SJW attenuate the signs of nicotine withdrawal in mice.[12] In another open-label study of SJW for tobacco cessation, SJW (at a dose of 900 mg per day for 3 months) showed a 24% (9/37) smoking abstinence rate at end of treatment amongst 24 cigarette smokers.[13]

Apart from depression and tobacco dependence it under trial for the treatment of raynauds phenomenon.[14] Another phase 3 trial has shown its promising role in the treatment of raynaud's phenomenon. It is hypothesized that SJW 300mg, 3 times a day will decrease the

frequency, duration and severity of raynaud's phenomenon attacks when compared to placebo. (Clinical Trials.gov Identifier: NCT00351117).

It is under various phases of clinical trial study for other conditions like for irritable bowel syndrome, social phobia, obsessive-compulsive disorder, generalized social anxiety disorder (GSAD), attention deficit hyperactive disorder (ADHD), in relieving fatigue in patients undergoing chemotherapy or hormone therapy for cancer.[14] St. John's wort may help in relieving fatigue in patients with cancer who are undergoing chemotherapy or hormone therapy.[14] But. St. John's wort has no significant effect on pain in polyneuropathy.[15] It has been mentioned in an Iranian study that, SJW has proved to be a folkore medicine for the treatment of rheumatism, haemorrhoids, neuralgia, sprains and snakebite also.[16] It is also used for its stimulant, spasmolytic, hypotensive, antibacterial, anti-inflammatory and antiviral action.[16] It has also shown anticonvulsant, antidiabetic and antioxidant effects in various animal screening methods.[16]

Flower of H. Perforatum has shown a concentration dependent and long- lasting inhibition of development of tumor cells and elevated the level of white blood cells.[16] This antitumor activity is the basis for its use in treatment of various cancers.[16] [23]

Tepkeeva et al 2008 demonstrated delayed appearance and growth of palpable breast cancer in mice.[16] [24]

Adverse effects of SJW

This herbal drug has fewer side effects than many conventional antidepressants and is better tolerated.[2] Adverse events that are frequently reported include nausea, headache, constipation, dizziness, confusion, fatigue, hair loss and dry mouth.[9] Serotonin syndrome might be resulted when St. John's wort is combined with sympathomimetics, antidepressants, or triptans.[17] Some photosensitive reactions that have been documented for St. John's wort which might be because of hypericin.[18] As with other antidepressant agents, St. John's wort has also been reported by Nierenberg AA et al 1999 to precipitate hypomania, mania, or an increased cycling of mood states, particularly in patients with occult bipolar disorder. Risk of hypericum-induced mania may be significant as this is a popular over-the-counter preparation.[19][20]

Drug interactions of SJW

SJW is a potent inducer of CYP3A4 which results in decreased efficacy of antiretrovirals, cyclosporine, tacrolimus, antiepileptics, irinotecan, and other chemotherapeutic agents.[9]

St. John's Wort increases the metabolism of norethindrone and ethinyl estradiol and showed higher incidences of breakthrough bleeding, follicle growth and ovulation. It should be used cautiously amongst women using oral contraceptives as it might interfere with contraceptive effectiveness.[21]

Boceprevir is generally prescribed along with interferon/ribavirin and depression has been described frequently in patients undergoing HCV treatment. Such patients might purchase over-the-counter herbals to manage depression. Thus the knowledge of interaction between SJW and Boceprevir is desirable.[22]

SJW is an inducer of CYP3A4 that is involved in the metabolism of the hepatitis C virus (HCV) protease inhibitor boceprevir. It was concluded the study that co-administration of multiple doses of SJW did not have a clinically significant impact on boceprevir plasma exposure. They suggested that SJW and boceprevir can be safely co-administered as Boceprevir increased hypericin C_{max} by only ~30%.[22]

CONCLUSION

SJW may offer promising role in the treatment of depression and other miscellaneous conditions like raynauds phenomenon, irritable bowel syndrome, social phobia, obsessive-compulsive disorder, generalized social anxiety disorder and many more. It should be given cautiously with certain drugs like antiretrovirals, cyclosporine, tacrolimus, antiepileptics, irinotecan and other chemotherapeutic agents because of its enzyme inducing properties. It might prove a potential drug target because of its antidiabetic, anticonvulsant, antioxidant and antitumor property.

FINANCIAL SUPPORT AND SPONSORSHIP: Nil.

FUNDING: Not applicable.

ACKNOWLEDGEMENTS: None declared.

REFERENCES

1. Hypericum perforatum Linn. In: Sharma R, eds. Medicinal plants of India- An encyclopedia. Daya publishing house. New Delhi. 2003; 131.
2. Antidepressants and antimanic drugs. In: Sharma HL, Sharma KK, eds. Principles of Pharmacology. 1st ed. Paras Publishing. New Delhi. 2007; 472.
3. Pradeep J. Nathan. Hypericum perforatum (St John's Wort): a non-selective reuptake inhibitor? A review of the recent advances in its pharmacology. J Psychopharmacol, January 2001; 15: 1 47-54.
4. St. John's wort is primarily metabolized by the liver. About the cover: St. John's wort. J Soc Integr Oncol. 2006 Winter; 4(1): 52-5.
5. Klier CM, Schmid-Siegel B, Schäfer MR, Lenz G, Saria A, Lee A, et al. St. John's wort (Hypericum perforatum) and breastfeeding: plasma and breast milk concentrations of hyperforin for 5 mothers and 2 infants. J Clin Psychiatry. 2006 Feb; 67(2): 305-9.
6. Linde K, Mulrow CD, Berner M. St John's wort for depression. Cochrane Database Syst Rev. 2005 Apr 18; (2): CD000448.
7. Linde K, Berner M, Egger M. St John's wort for depression Meta-analysis of randomised controlled trials. The British Journal of Psychiatry, Jan 2005; 186(2): 99-107.
8. Linde, K., Ramirez, G., Mulrow, C. D., et al St John's wort for depression - an overview and meta-analysis of randomised clinical trials. BMJ 1996; 313: 253 -58.
9. About the cover: St. John's wort. J Soc Integr Oncol. 2006 Winter; 4(1): 52-5.
10. Shelton, R. C., Keller, M. B., Gelenberg, A., et alEffectiveness of St John's wort in major depression. A randomized controlled trial. JAMA 2001; 285: 1978 -86.
11. Sood A, Ebbert JO, Prasad K, Croghan IT, Bauer B, Schroeder DR.A randomized clinical trial of St. John's wort for smoking cessation. J Altern Complement Med. 2010 Jul; 16(7): 761-7.
12. Catania MA, Firenzuoli F, Crupi A, Mannucci C, Caputi AP, Calapai G. Hypericum perforatum attenuates nicotine withdrawal signs in mice. Psychopharmacology (Berl). 2003 Sep; 169(2): 186-9.
13. Lawvere S. Mahoney MC. Cummings KM, et al. The efficacy of St. John's Wort for smoking cessation: A pilot study. World Congress on Tobacco or Health; Aug; Helsinki, Finland. 2003.
14. ClinicalTrials.gov. St Johns Wort. Available from: https://clinicaltrials.gov/st johns wort. [Last accessed on 2015 December 29].

15. Sindrup SH, Madsen C, Bach FW. St. John's wort has no effect on pain in polyneuropathy. Pain. 2001 Apr; 91(3): 361-5.

a. Jinous. Phytochemistry, pharmacology and medicinal properties of Hypericum perforatum L. Afr J Pharm Pharmacol. 2010; 6(9): 1387-94.

16. Parker V, Wong AH, Boon HS. Adverse reactions to St John's Wort. Can J Psychiatry. 2001 Feb; 46(1): 77-9.

17. Barnes J, Anderson LA, Phillipson JDSt John's wort (Hypericum perforatum L.): a review of its chemistry, pharmacology and clinical properties. J Pharm Pharmacol. 2001 May; 53(5): 583-600.

18. Nierenberg AA, Burt T, Matthews J. Mania associated with St. John's wort. Biol Psychiatry. 1999 Dec 15; 46(12): 1707-8.

19. Güzelcan Y, Scholte WF, Assies J. Mania during the use of a combination preparation with St. John's wort (Hypericum perforatum). Ned Tijdschr Geneeskd. 2001 Oct 6; 145(40): 1943-5.

20. Murphy PA, Kern SE, Stanczyk FZ,. Interaction of St. John's Wort with oral contraceptives: effects on the pharmacokinetics of norethindrone and ethinyl estradiol, ovarian activity and breakthrough bleeding. Contraception. 2005 Jun; 71(6): 402-8.

21. Jackson A, D'Avolio A, Moyle G, Bonora S, Di Perri G, Else Let al. Pharmacokinetics of the co-administration of boceprevir and St John's wort to male and female healthy volunteers. J Antimicrob Chemother. 2014 Jul; 69(7): 1911-5.

22. Roscetti G, FranzeseO, Comandini A, Bonmassar E. Cytotoxic activity of Hypericum perforatum L. On K62 erythroleukemic cells: differential effects between methanolic extract and hypericin. Phytother. Res., 18(1): 66-72.

23. Tepkeeva II, Moiseeva EV, Chaadaeva AV, Zhavoronkova EV, Kessler YV, Semus hina SG, et al. Evaluation of antitumor activity of peptide extracts from medicinal plants on the model of transplanted breast cancer in CBRB-Rb(8,17) 1lem mice. Bull. Exp. Boil. Med. 14(4): 464-66.