



Received on 30 May, 2015; received in revised form, 24 July, 2015; accepted, 29 September, 2015; published 01 December, 2015

## THERAPEUTIC POTENTIAL OF *HYPERICUM PERFORATUM*: A REVIEW

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### Keywords:

*Hypericum perforatum*, St. John's wort, Anti-depressant agent, Hypericins, Hyperforins.

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**ABSTRACT:** The irreversible effects of modern therapies and increasing drug resistance have augmented our reliance on medicinal plants for herbal remedy against the deadly and infectious diseases. *Hypericum perforatum* or St. John's wort (SJW) family Clusiaceae has been used to treat depression, mental disorders, wounds, peptic ulcers, malaria, gout and arthritis. Various compounds of the plant are known as sedative, diuretic and expectorant according to their effects. The flowers and the aerial parts are commonly used in the preparations of traditional medicines. *Hypericum perforatum* with identified active compounds like Hypericins, Hyperforins is being studied for its anti-depressant activity in both humans and animals. It is also used in the treatment of pulmonary complaints, bladder troubles in suppression of urine, dysentery, worms, diarrhoea, hysteria and other haemorrhages and jaundice. Most of its therapeutic effects with mechanism of action are critically reviewed in the present paper.

**INTRODUCTION:** The Genus *Hypericum* L. (Guttiferae/Clusiaceae/Hypericaceae) containing 465 species globally<sup>41, 48, 49</sup> is a large family of plants with potential medicinal value. However, *H. perforatum* is mainly studied for its bioactivities due to its popularity among the depression patients. *Hypericum perforatum* commonly known as St. John's wort is named so because of the traditional collection of its flower at the feast of St. John the Baptist on June 24<sup>th</sup><sup>48</sup>. It is a perennial herb native to Asia and Europe<sup>4, 38</sup> but known globally for its traditional and modern uses. The use of this species as an herbal remedy to treat a variety of internal and external ailments dates back to the time of the ancient Greeks.

Since then, it has remained a popular treatment for anxiety, infection, and wound healing<sup>38, 56, 57</sup>. In last couple of decades, the majority of research on *H. perforatum* was based on its use as anti-depressant, which has expanded its popularity and made it among the top selling dietary supplements in the market<sup>4, 14</sup>. Pharmaceutical companies, particularly in Europe, prepare standard formulations of this herb that are taken by millions of people. Moreover, it has also attracted the scientists' brain for its anti-inflammatory and antimicrobial properties against the inflammatory diseases<sup>14, 24</sup>.

Recent research suggests the effectiveness of this herb in treating other ailments including cancer, inflammation related disorders, and bacterial and viral diseases, and used as an antioxidant and neuro-protective agent. Of the total 400 species, distributed in the temperate regions of the world, about 25 species are found in the Indian Himalayan Region (IHR). Amongst the species, *Hypericum perforatum*, grows in Himalayas at higher altitudes

<p><b>QUICK RESPONSE CODE</b></p> 	<p><b>DOI:</b> 10.13040/IJPSR.0975-8232.6(12).4982-88</p> <hr/> <p>Article can be accessed online on: <a href="http://www.ijpsr.com">www.ijpsr.com</a></p> <hr/> <p>DOI link: <a href="http://dx.doi.org/10.13040/IJPSR.0975-8232.6(12).4982-88">http://dx.doi.org/10.13040/IJPSR.0975-8232.6(12).4982-88</a></p>
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and in the central parts of the country, is a prospective herb to be used as a anti-depressant, anti-cancer, anti-tumour and anti-viral agent. Considering its anti-viral property, the plant is widely studied for its effect against the HIV species. Some biologically active constituents like hyperforin and adhyperforin (phloroglucinols), hypericin and pseudohypericin (naphthodianthrones), flavonoids, xanthenes, oligomeric procyanidines, and amino acids have been detected in *Hypericum*<sup>4,38</sup>.

### Botanical Description:

The genus name *Hypericum* is derived from the Greek words *hyper* (above) and *eikon* (picture), in reference to the plant's traditional use in warding off evil by hanging plants over a religious icon in the house during St John's day (24<sup>th</sup> June). The species name *perforatum* refers to the presence of small oil glands in the leaves that look like windows, which can be seen when they are held against the light<sup>33</sup>. *Hypericum* consists of herbs and shrubs having yellow or coppery flowers with four to five petals, numerous stamens, and a single pistil<sup>10</sup> and free branching typically range from 40 to 80 cm in height<sup>16,36</sup>. The stems and branches are densely covered by oblong, smooth margined leaves that range from 1 to 3 cm long and 0.3-1.0 cm wide. The leaves are interrupted by minute translucent spots that are evident when held up to the light. The upper portions of mature plants can produce several dozen five petaled yellow flowers that are typically 1.0-2.0 cm wide. The edges of the petals are usually covered with black dots. Crushed flowers produce a blood red pigment. By late summer, the flowers produce capsules that contain dozens of tiny, dark brown seeds. It thrives in poor soils, and is commonly found in meadows, fields, waste areas, roadsides, and abandoned mines and quarries<sup>16,27,36</sup>. Due to concerns over phototoxicity to livestock, *H. perforatum* is listed as a noxious weed in seven western states in the United States. Programs promoting its eradication are underway in Canada, California, and Australia.

### Chemical Constituents:

Chemical investigations have detected seven groups of medicinally active compounds in *H. Perforatum*<sup>38</sup>. They include naphthodianthrones, phloroglucinols, and flavonoids (such as

phenylpropanes, flavonol glycosides, and biflavones), as well as essential oils<sup>2,4,11,46</sup>. There two major active constituents have been identified: hypericin (a naphthodianthron) and hyperforin (a phloroglucinol).

### Naphthodianthrones:

The class of compounds isolated from *H. perforatum* and the one which is the most researched naphthodianthrones<sup>17,18,47</sup>. They include hypericin, pseudohypericin, isophypericin, and protohypericin<sup>2,11</sup>. Of these, hypericin—an anthraquinone derived pigment that is responsible for the red color of SJW oils. Hypericin is found in the flowers in the form of black dots that are located along the petals. Due to its chemical structure, hypericin is highly photoreactive.

### Flavonoids:

Flavonoids in SJW range from 7% in stems to 12% in flowers<sup>11</sup> and leaves<sup>18</sup>. Flavonoids include flavonols (kaempferol, quercetin), flavones (luteolin), glycosides (hyperside, isoquercitrin, and rutin), biflavones (biapigenin), amentoflavone, myricetin, hyperin, oligomeric proanthocyanadins, and miquelianin, all of which are biogenetically related<sup>2,47</sup>.

### Lipophilic compounds:

Extracts of SJW contain several classes of lipophilic compounds with demonstrated therapeutic value, including phloroglucinol derivatives and oils. Hyperforin, isolated in concentrations of 24.5%<sup>8,47</sup>, is a prenylated phloroglucinol. Hyperforin is unstable in the presence of both light and oxygen<sup>23</sup>. Other phloroglucinols include adhyperforin (0.2% 1.9%), furohyperforin, and other hyperforin analogs<sup>2,11,18,21</sup>. Essential oils are found in concentrations ranging from 0.05% to 0.9%<sup>21</sup>. They consist mainly of mono and sesquiterpenes, specifically 2-methyloctane, nonane,  $\alpha$  and  $\beta$  pinene,  $\alpha$  terpineol, geranyl, and trace amounts of myrecene, limonene, and caryophyllene<sup>21,46</sup>.

### Additional compounds:

These include tannins (ranging from 3% to 16%), xanthenes (1.28 mg/100g), phenolic compounds (caffeic acid, chlorogenic acid, and pcoumaric acid), and hyperfolin. Additional compounds

include acids (nicotinic, myristic, palmitic, and stearic), carotenoids, choline, pectin, hydrocarbons, and long chain alcohols<sup>11</sup>.

### Pharmacological activities:

#### Anti-depressant:

St. John's wort (*Hypericum perforatum* L.) has been used for centuries to treat a number of common ailments (such as neuralgia, sleep disorders, wound healing, and hemorrhoids), but it is best known for its use in the treatment of mild to moderate depression<sup>39</sup>.

#### Responsible Compounds:

SJW is known to have several active ingredients including cyclopseudohypericin, hypericin, hyperforin, isohypericin, protohypericin, pseudohypericin and several other flavonoids<sup>5, 13</sup>. Each of these active components appears to have differing levels of contribution to its anti-depressant properties<sup>5</sup>.

**Mechanism of action:** One of the proposed mechanisms of St. John's wort in the treatment of

depression is the inhibition of the uptake of serotonin (5HT), dopamine (DA) and norepinephrine (NE) from the synaptic cleft of interconnecting neurons<sup>8, 40</sup>. A second contributing mechanism is the ability to bind to the major neuro-inhibitory receptor, gamma amino butyric acid (GABA A and GABA B) receptors, to block the binding of GABA<sup>3, 54</sup>. This reduction in GABA ligand binding results in decreased central nervous system (CNS) depression. A third mechanism is an increase in the number or density of 5HT2 receptors in the frontal cortex of the brain, which is potentially beneficial when treating depression<sup>37</sup>.

A fourth and possibly fifth separate contributing mechanism is St. John's wort ability to inhibit the activity of both monoamine oxidase (MAO) and catechol O-methyl transferase (COMT) enzymes<sup>37, 55</sup>. Active form of both of these CNS enzymes metabolize dopamine precursors into inactive products and allows dopamine to metabolize to norepinephrine (NE) in the brain. Thus, inhibition of these enzymes in the CNS favors the metabolism of Dopamine and the formation of NE (**Fig.1**).

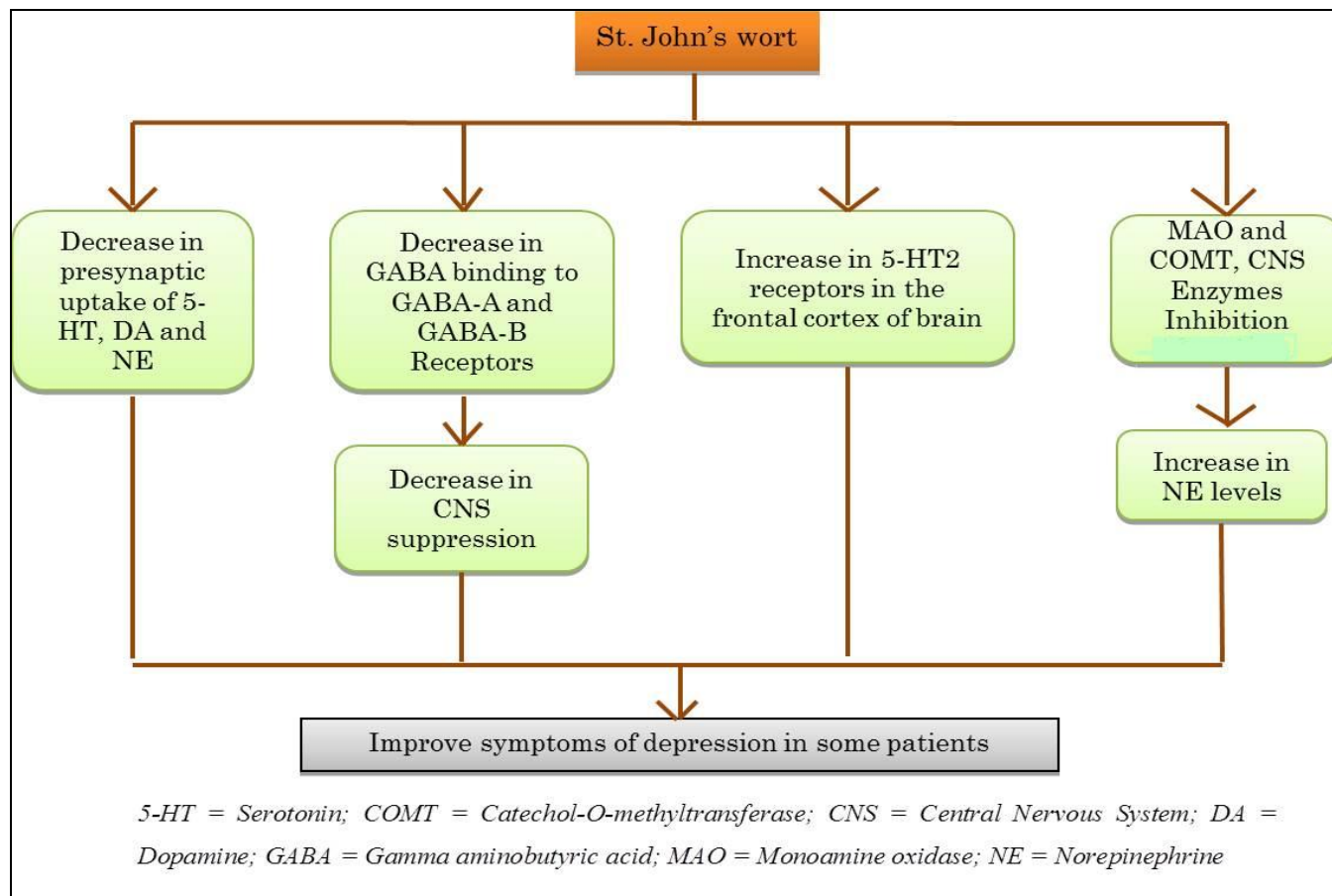


FIG.1: ANTI-DEPRESSIVE MECHANISM OF ST. JOHN'S WORT EXTRACT (SJW).

**Anti-bacterial and anti-viral:**

Extracts of *H. perforatum* have been used to treat cuts, abrasions, and other wounds for thousands of years. It is useful in reducing inflammation and is well known for its ability to serve as an antibacterial agent. Hyperforin, the main antibacterial component was determined to inhibit the growth of certain types of microorganisms especially for all Gram positive bacteria. However, no growth inhibitory effects were seen in the Gram negative bacteria<sup>6</sup>.

The SJW extracts have long been regarded as being effective against various classes of viruses. Flavonoid and catechin containing fractions of SJW are active against influenza virus<sup>34</sup>. Hypericin inactivates enveloped viruses at different points in their life cycle<sup>28</sup>, and their fusion with cell membranes<sup>10, 28</sup>. Considering to that Hypericin is used as natural candidate to inactivate several enveloped viruses present in human blood and also to treat Acquired Immunodeficiency Syndrome (AIDS) patients<sup>22, 33</sup>. Other reverse-transcribed viruses like hepatitis virus B and C (HBV and HCV) have been found to be inhibited by hypericin *in vitro*<sup>37, 55</sup>. It was found hypericin ineffective against the hepatitis C virus in a doses study<sup>25</sup>.

Some recent reports showed that isoquercetrin in *H. perforatum* extract could inhibit H1N1 influenza virus replication in MDCK cells. However, most observations of anti-viral activity of *Hypericum* were acquired from *in vitro* studies and a limited number of animal studies, while human clinical trials often showed little or no significant effect. Studies on other viruses have shown the hypericin induced *in-vitro* inactivation of Bovine Diarrhea Virus (BVDV) in the presence of light<sup>43</sup>.

**Anti HIV Property:**

Hypericin induces changes in p24 protein and the p24 containing gag precursor, p55 and the formation of an anti p24 immuno-reactive material which inhibit the release of reverse transcriptase activity<sup>10</sup>. However, in a phase I clinical trial, it was found that hypericin had no beneficial effect on administration to 30 HIV infected patients with CD4 counts less than 350 cells/mm<sup>3</sup><sup>20</sup>. Recently, in a study, 3- hydroxy lauric acid was found in the

field grown *H. perforatum* which has shown better anti HIV activity<sup>43</sup>.

**Mechanism of action:**

With no apparent effect on viral nucleotide, transcription and translation being observed, the authors speculated that the anti-viral mechanism of the *Hypericum* was having a direct interference with virus infection and shedding, or inactivation of virus, or disruption of lipid membrane of virus. However, conclusive clinical evidence has yet to be found to support the *in vivo* efficacy of hypericin and *H. perforatum* against HIV.

The Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway are responsible for transmitting signals from a myriad of cytokine and hormone receptors<sup>45</sup>. Negative regulation of the JAK/STAT pathway is carried out through suppressor of cytokine signaling (SOCS) proteins, whose transcription is controlled by STATs<sup>44</sup>. Although SOCSs are important to contain inflammation, which are manipulated by pathogens such as influenza virus by regulating SOCS3 expression but there are certain biological components found in *H. perforatum* extract which may inhibit the viral infection.

**Anticancer:**

Hyperforin and hypericin have also been examined for their anticancer properties. Hyperforin inhibits tumor cell growth *in vitro*<sup>51</sup>. Studies demonstrated that hyperforin in conjunction with polyphenolic procyanidin B2 effectively inhibited the growth of leukemia in K562 and U937 cells, brain glioblastoma cells LN229, and normal human astrocytes<sup>23</sup>. Hypericin also inhibits the growth of cells derived from a variety of neoplastic tissues, including glioma, neuroblastoma, adenoma, mesothelioma, melanoma, carcinoma, sarcoma, and leukemia<sup>15</sup>. Hypericin being photodynamic compound within photoactivated with white light or ultraviolet light or both could induce nearly complete apoptosis (94%) in malignant cutaneous T cells and lymphoma T cells<sup>15</sup>. Exposing tumors cells to hypericin in conjunction with laser irradiation led to toxic effects on human prostatic cancer cell lines<sup>9</sup>, human urinary bladder carcinoma cells<sup>26</sup>, and pancreatic cancer cell lines<sup>29</sup> in *in-vitro* systems.

As a matter of attention, hypericin alone has only a weak inhibitory effect on cancerous cell growth, whereas methanolic extract of SJW together with hypericin leads to long lasting inhibition of cell growth, induces apoptosis, and decreases phototoxicity<sup>50, 52</sup>. Considering the encouraging results of hyperforin and hypericin as anticancer agents, more research is needed to evaluate their efficacy, mode of action, and adverse interactions.

**Mechanism of action:** The mechanism involves induction of apoptosis (programmed cell death) through the activation of caspases, which are cysteine proteases that trigger a cascade of proteolytic cleavage in mammalian cells. Hypericin with its greater photodynamic properties<sup>1</sup> acts as a powerful natural photosensitizer in the presence of oxygen and light. It generates superoxide radicals that form peroxide or hydroxyl radicals, or singlet oxygen molecules that kill tumor cells. Hence, in future, hypericin can be used as a component of photodynamic therapy (PDT).

#### **Neuroprotective:**

*H. perforatum* serves as a neuroprotective agent against MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) induced Parkinson's disease in mice<sup>35</sup>. *H. perforatum* extract led to the inhibition of MAOB (monoamine oxidase B) activity and decreased astrocyte activation in striatal area of (MPTP) induced mice. The flavonols quercetin and kaempferol provide neuroprotective action by decreasing oxidation of the mitochondrial lipid membrane and maintaining mitochondrial transmembrane electric potential<sup>53</sup>. They lower the ability of mitochondria to absorb calcium. Extracts of SJW protect against cell death caused by amyloid P peptides (Abeta) that form plaques in the brains of those suffering from Alzheimer's disease. Hypericin may interfere with the processes of polymerization of the beta-amyloid peptide responsible for the onset of Alzheimer's disease<sup>19</sup>.

#### **Other Activities:**

*H. perforatum* shows promise as an anti-inflammatory agent. Rats fed doses of SJW showed decreased levels of blood and bowel enzymes associated with colonic inflammation<sup>12</sup>, and had lower incidences of gastric ulcers<sup>12</sup>.

The extracts of *H. perforatum* decrease oxidative stress and consequently prevent neurotoxicity, inflammation, and gastrointestinal problems. *H. perforatum* extract has been used over thousands of years as a wound healing agent. The chicken embryonic fibroblasts exposed to SJW extract enhanced collagen production, followed by the polygonal shape activation of fibroblast cells that is responsible for wound closure<sup>42</sup>.

#### **Future Perspectives:**

In recent years, many studies have proven the efficacy of some HP extracts in the treatment of depression, bacterial and viral infection, neurological disorders, etc. It has also received special attention due to its pharmacological properties, including antiseptic, spasmolytic, tonic, diuretic and anesthetic remedies. Despite the dozens of clinical, *in vivo*, and *in vitro* studies conducted on the medicinal attributes of SJW, several unanswered questions still prevail regarding its therapeutic value, mechanisms of action, and adverse interactions. The future research must focus on resolving the apparent contradictions related to this herbal plant. Additional research is needed regarding the therapeutic value of SJW as anti-cancerous, anti-HIV, immuno-modulatory agent and so on. Moreover, the potency of hypericin, hyperforin, and flavonoids must be further elucidated.

Anti-bacterial property of SJW is reported against the Gram positive bacteria but it is still to be thoroughly studied against the Gram negative bacteria. Hypericin was tested as anti-HIV drug, but some more studies are required to understand its mechanism of action and efficacy in serious AIDS patients. The anti-retroviral activity of 3-hydroxy lauric acid reported to be found in the field grown SJW extract may further be studied for its *in-vivo* effects. As anti-cancer agent evaluation of efficacy, mode of action and adverse effects of hypericin and hyperforin is needed.

#### **REFERENCES:**

1. Agostinis P, Vantieghe A, Merlevede W, de Witte PAM: Hypericin in cancer treatment: More light on the way. *Int J Biochem Cell Biol* 2002; 34:221-41.
2. Barnes J, Anderson LA, Phillipson JD: *St. John's wort (Hypericum perforatum L.): A review of its chemistry,*

- pharmacology, and clinical properties. *J Pharm Pharmacol* 2001; 53:583–600.
3. Baureithel KH, Buter KB, Engesser A et al: Inhibition of benzodiazepine binding in vitro by amentoflavone, a constituent of various species of *Hypericum*. *Pharm Acta Helv* 1997; 72:15-37.
  4. Bombardelli E, Morazzoni P: *Hypericum perforatum*. *Fitoterapia* 1995; 66(1):43-68.
  5. Butterweck V: Mechanism of action of St John's wort in depression: what is known? *CNS Drugs* 2003; 17:53962.
  6. Bystrov NS, Chernov BK, Dobrynin VN, Kolosov MN: The structure of hyperforin. *Tetrahedron Lett* 1975; 32:2791–4.
  7. Cayci MK, Dayioglu H: *Hypericum perforatum* extracts healed gastric lesions induced by hypothermic restraint stress in Wistar rats. *Saudi Med J* 2009; 30(6):750–4.
  8. Chatterjee S, Bhattacharya SK, Wonnemann M and Singer A, Muller WE: Hyperforin as possible antidepressant component of *Hypericum* extracts. *Life Sci* 1998; 63:499–510.
  9. Colasanti A, Kisslinger A, Liuzzi R et al: Hypericin photosensitization of tumor and metastatic cell lines of human prostate. *J Photochem Photobiol* 2000; 54:103–7.
  10. Degar S, Prince AM, Pascual D et al: Inactivation of the human immunodeficiency virus by hypericin: Evidence for photochemical alterations of p24 and a block in uncoating. *AIDS Res Hum Retroviruses* 1992; 8:1929–36.
  11. Der Marderosian A, Beutler J: *The Natural Review of Products*. St. Louis, MO: Facts and Comparisons 2002.
  12. Dost T, Ozkayran H, Gokalp F, Yenisey C, Birincioglu M: The effect of *Hypericum perforatum* (St. John's Wort) on experimental colitis in rat. *Dig Dis Sci* 2009; 54(6):1214–21.
  13. Ebadi M: *Pharmacodynamic basis of herbal medicine*. 2nd Ed. Taylor & Francis Group. Boca Raton, FL. 2007.
  14. Erdelmeier CAJ: Hyperforin, possibly the major non-nitrogenous sec-metabolite of *Hypericum perforatum* L. *Pharmacopsychiatry* 1998; 31:2-6.
  15. Fox FE, Niu Z, Tobia A, Rook AH: Photoactivated hypericin is an anti-proliferative agent that induces a high rate of apoptotic death of normal, transformed, and malignant T lymphocytes: Complications for the treatment of cutaneous lympho-proliferative and inflammatory disorders. *J Invest Dermatol* 1998; 111(2):327–32.
  16. Gleason HA, Cronquist A: *Manual of Vascular Plants of Northeastern United States and Adjacent Canada*. 2nd ed. Bronx, NY: The New York Botanical Garden; 1991.
  17. Grainger Bisset N, Wichtl M: *Herbal Drugs and Phytopharmaceuticals*. 2nd ed. Stuttgart, Germany: Medpharm GmbH Scientific Publishers; 2001.
  18. Greeson JM, Sanford B, Monti DA: St. John's wort (*Hypericum perforatum*): A review of the current pharmacological, toxicological, and clinical literature. *Psychopharmacology* 2001; 153:402–14.
  19. Griffith TN, Varela-Nallar L, Dinamarca MC, Inestrosa NC: Neurobiological effects of Hyperforin and its potential in Alzheimer's disease therapy. *Curr Med Chem* 2010; 17:391-406.
  20. Gulick RM, McAuliffe V, Holden Wiltse J et al: Phase I studies of hypericin, the active compound in St. John's wort, as an antiretroviral agent in HIV infected adults. *AIDS Clinical Trials Group Protocols 150 and 258. Ann Intern Med* 1999; 130:510–4.
  21. Hahn G: *Hypericum perforatum* (St. John's wort): A medicinal herb used in antiquity and still of interest today. *J Naturopathic Med* 1992; 3:94–6.
  22. Holden C: Treating AIDS with worts. *Science* 1991; 254:522.
  23. Hostanska K, Reichling J, Bommer S, Weber M, Saller R: Hyperforin a constituent of St John's wort (*Hypericum perforatum* L.) extract induces apoptosis by triggering activation of caspases and with hypericin synergistically exerts cytotoxicity towards human malignant cell lines. *Eur J Pharm Biopharm* 2003; 56(1):121–32.
  24. Hudson JB, Lopez-Bazzocchi I, Towers GH: Antiviral activities of Hypericin. *Antiviral Research* 1991; 15: 101-112.
  25. Jacobson JM, Feinman L, Liebes L et al: Pharmacokinetics, safety, and antiviral effects of hypericin, a derivative of St. John's wort plant, in patients with chronic hepatitis C virus infection. *Antimicrob Agents Chemother* 2001; 45:517–24.
  26. Kamuhabwa AR, Agostinis P, D'Hallewin MA, Kasran A, de Witte PA: Photodynamic activity of hypericin in human urinary bladder carcinoma cells. *Anticancer Res* 2000; 220:2579–84.
  27. Klemow KM, Raynal DJ: Population biology of an annual plant in a temporally variable habitat. *J Ecol* 1983; 71:691–703.
  28. Lenard J, Rabson A, Vanderoef R: Photodynamic inactivation of infectivity of human immunodeficiency virus and other envelope viruses using hypericin and rose bengal: Inhibition of fusion and syncytia formation. *PNAS* 1993; 90:158–62.
  29. Liu CD, Kwan D, Saxton RE, McFadden DW. Hypericin and photodynamic therapy decreases human pancreatic cancer in vitro and vivo. *J Surg Res* 2000; 93:137–43.
  30. Liu F, Pan C, Drumm P, Ang CY: Liquid chromatography mass spectrometry studies of St. John's wort methanol extraction: Active constituents and their transformation. *J Pharm Biomed Anal* 2005; 37:303–12.
  31. Maury W, Price JP, Brindley MA: Identification of light independent inhibition of human immunodeficiency virus I infection through bioguided fractionation of *Hypericum perforatum*. *Virology* 2009; 6:101.
  32. Mehta S: "Pharmacognosy of St. John's Wort". [Pharmaxchange.info](http://Pharmaxchange.info). Retrieved 2014; 02-16.
  33. Meruelo D: The potential use of hypericin as inactivator of retroviruses and other viruses in blood products. *Blood* 1993; 82:205A.
  34. Mishenkova EL, Derbentseva NA, Garagulya AD, Litvin LN: Antiviral properties of St. John's wort and preparations produced from it. *Transactions of the Congress of Microbiologists of the Ukraine* 1975; 4:222–322.
  35. Mohanasundari M, Sabesan M: Modulating effect of *Hypericum perforatum* extract on astrocytes in MPTP induced Parkinson's disease in mice. *Eur Rev Med Pharmacol Sci* 2007; 11(1):17–20.
  36. Muenscher WC: *Weeds*. New York: The MacMillan Company; 1946.
  37. Muller WE, Rolli M, Schafer C et al: Effects of *Hypericum* extract (LI 160) in biochemical models of antidepressant activity. *Pharmacopsychiatry* 1997; 30 Suppl 2:102-7.
  38. Nahrstedt A, Butterwick V: Biologically active and other chemical constituents of the herb *Hypericum perforatum* L. *Pharmacopsychiatry* 1997; 30:129–34.
  39. National Center for Complementary and Alternative Medicine: National Institutes of Health. Herbs at a glance: St. John's wort. Last accessed on 12/2009:NCCAM
  40. Neary JT, Bu Y: *Hypericum* LI 160 inhibits uptake of serotonin and norepinephrine in astrocytes. *Brain Res* 1999; 816:358-63.
  41. Nogueira T, Marcelo-Curto MJ, Figueiredo AC, Barroso JG, Pedro LG, Rubiolo P, Bicchi C: Chemotaxonomy of

- Hypericum genus from Portugal: Geographical distribution and essential oils composition of *Hypericum perforatum*, *Hypericum humifusum*, *Hypericum linarifolium* and *Hypericum pulchrum*. Biochemical Systematics and Ecology 2008; 36(1):40-50.
42. Ozturk N, Korkmaz S, Ozturk Y: Wound healing activity of St. John's Wort (*Hypericum perforatum* L.) on chicken embryonic fibroblasts. J Ethnopharmacol 2007; 111(1):33-9.
  43. Prince AM, Pascual D, Meruelo D et al: Strategies for evaluation of enveloped virus inactivation in red cell concentrates using hypericin. Photochem Photobiol 2000; 71:188-95.
  44. Qin H, Roberts KL, Niyongere SA, Cong Y, Elson CO, Benveniste EN: Molecular mechanism of lipopolysaccharide-induced SOCS-3 gene expression in macrophages and microglia. Journal of Immunology 2007; 179(9):5966-5976.
  45. Rawlings JS, Rosler KM, Harrison DA: The JAK/STAT signaling pathway. Journal of Cell Science 2004; 117(Pt 8):1281-1283.
  46. Reuter H: Chemistry and biology of *Hypericum perforatum* (St. John's wort) ACS Symp Ser 1998; 691:287-98.
  47. Robbers J, Tyler VE: Tyler's Herbs of Choice: The Therapeutic Use of Phytomedicinals. New York: Haworth Press; 1999.
  48. Robson NKB: Studies in the genus *Hypericum* L. (Guttiferae). I. Infrageneric classification. 1977; Vol. 5, p 293.
  49. Robson NKB: Studies in the genus *Hypericum* L. (Clusiaceae). Section 9, *Hypericum sensu lato* (part 3): subsection 1, *Hypericum* series 2, *Senanensia*: subsection 2, *Erecta* and section 9b, *Graveolentia*. Syst Biodivers 2006; 4(1):19-98.
  50. Roscetti G, Franzese O, Comandini A, Bonmassar E: Cytotoxic activity of *Hypericum perforatum* L. on K562 erythroleukemic cells: Differential effects between methanolic extract and hypericin. Phytother Res 2004; 18(1):66-72.
  51. Schempp CM, Kirkin V, Simon Haarhaus B et al: Inhibition of tumour cell growth by hyperforin, a novel anticancer drug from St. John's wort that acts by induction of apoptosis. Oncogene 2002; 21:1242-50.
  52. Schmitt LA, Liu Y, Murphy PA, Petrich JW, Dixon PM, Birt DF: Reduction in hypericin-induced phototoxicity by *Hypericum perforatum* extracts and pure compounds. J Photochem Photobiol 2006; B 85 2 118 30.
  53. Silva B, Oliveira PJ, Dias A, Malva JO: Quercetin, kaempferol and biapigenin from *Hypericum perforatum* are neuroprotective against excitotoxic insults. Neurotox Res 2008; 13(34):265-79.
  54. Simmen U, Higelin J, Berger Buter K et al: Neurochemical studies with St. John's wort in vitro. Pharmacopsychiatry 2001; 34 Suppl 1:S137-42.
  55. Thiede HM, Walper A: Inhibition of MAO and COMT by *Hypericum* extracts and hypericin. J Geriatr Psychiatry Neurol 1994; 7 Suppl 1:S546.
  56. Wagner H, Bladt S. Pharmaceuticals quality of *Hypericum extracts*. Journal of Geriatric Psychiatry and Neurology 1994; S65-S68.
  57. Zdunek K, Alfermann W: Initiation of shoot organ cultures of *Hypericum perforatum* and formation of hypericin derivatives. Planta Medica 1992; 58: 621-625.

**How to cite this article:**

Shrivastava M and Dwivedi LK: Therapeutic Potential of *Hypericum Perforatum*: A Review. Int J Pharm Sci Res 2015; 6(12): 4982-88. doi: 10.13040/IJPSR.0975-8232.6(12).4982-88.

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