

Drug Interaction of *Hypericum Perforatum* with Routine Chemical Drugs

Reza Assadzadeh¹, Shabnam Shamaei², Aliasghar Manouchehri³

¹Assistant Professor of Nephrology, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran, ²Assistant Professor, Department of Chemistry, Islamic Azad University, Khorramabad Branch, Khorramabad, Iran,

³Assistant Professor, Department of Internal Medicine, Shahid Beheshti Hospital, Babol University of Medical Sciences, Babol, Iran

Abstract

In traditional medicine, *Hypericum perforatum* L. is used as an antidepressant, diuretic, analgesic, antiseptic and wound healing, anticonvulsant, rheumatism and chronic gastrointestinal spasms, abortion, sciatica, and for the treatment of infectious diseases such as syphilis, tuberculosis, dysentery, pertussis, worm excretion, and malaria. *H. perforatum* interferes with cardiac drugs, anesthetics, narcotics and analgesics, antibiotics, hormonal compounds, antiviral compounds, anticonvulsants and antidepressants, organ transplantation compounds, and iron compounds. Despite the medicinal effects of the valuable plant *H. perforatum*, the single use of this plant is very effective and valuable in the treatment of diseases and disorders, but its use with other chemical drugs due to the occurrence of drug interactions requires caution in consumption.

Keywords: Medicinal plant, *Hypericum perforatum*, Drug interaction, Chemical drug

Introduction

Hypericum perforatum L. is a plant of the Hypericaceae family. This plant is a valuable herbal medicine for humans and a dangerous weed for livestock [1, 2]. This plant is an herbaceous and perennial plant and has many herbaceous and permanent stems of 50 to 100 cm, the cross section of the spherical stem and has two protrusions. Flowering stems that emerge from the crown every year and are usually red and have many branches at the end. The leaves of this plant are petiole less, opposite, elongated, with rounded ends and without cuts. The leaves have three types of broad leaves, narrow leaves and medium leaves [3, 4]. In traditional medicine, *H. perforatum* is used as an antidepressant, diuretic, analgesic, antiseptic and wound healing, anticonvulsant, rheumatism and chronic gastrointestinal spasms, abortion, sciatica, for the treatment of infectious diseases such as syphilis, tuberculosis, dysentery, pertussis, worm repellent, malaria [5, 6]. It grows mostly in Europe, from Siberia to northwest China, Asia Minor, the Mediterranean, North Africa, Canada and Australia. In Iran, it grows in the north, northwest, northeast and west, Fars, Kohkiluyeh and Alborz Mountains [7].

This plant contains compounds such as flavonoids such as epigallocatechin, rutin, hyperoside, isoquercetin, quercetin, quercetin, amentoflavone, biopogenin, astilbin, myricetin, myclinin, kampferrol and lutolin. Phenolic acids such as chlorogenic acid, caffeic acid, picro maric acid, folic acid, p-hydroxybenzoic acid. Fluoroglucinols such as hyperforin and adiporphorin. Tannin compounds, volatile oils such as 2-methyl octane, non-oxane, 2-methyldecane, non-sodium, α -pinene, β -pinene, α -terpinol, geraniol, myrcene, limonene, caryophyllene and humolen. Saturated fatty acids such as isovaleric acid (3-methylbutanoic acid), palmitic acid, myricic acid and stearic acid. Alkanols such as 1-tetrasuzanol and 1-hexacosanol. Vitamins and their analogues are other constituents of the herb tea such as carotenoids, choline, nicotinamide, nicotinic acid [8-13].

Methodology For Review

In this study, relevant articles from ISI, PabMed, Scopus, google scholar, Magiran and ISC. databases were searched and related articles were used for review.

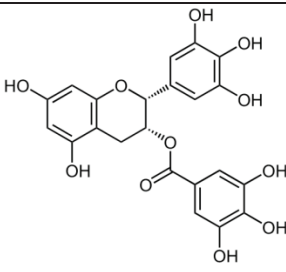
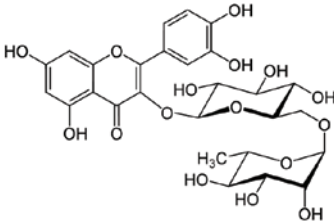
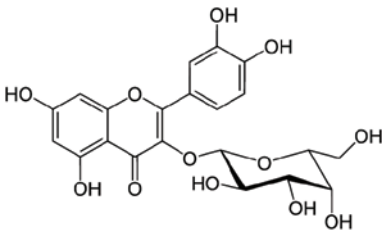
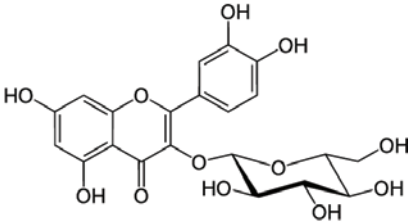
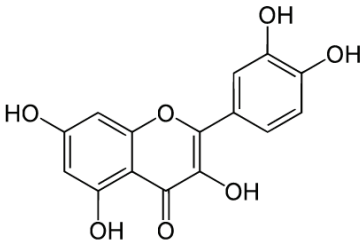
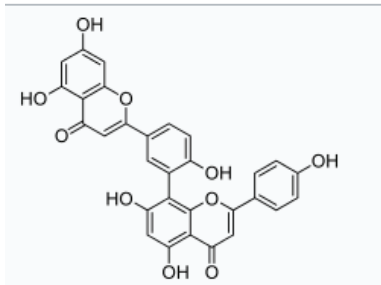
Results

As shown in Table 1, *Hypericum perforatum* has drug interactions with a number of chemical drugs.

Table 1. Drug Interaction of *Hypericum perforatum* with Chemical Drugs

Plant	Interfering drug	Interference type	Ref.
Plant name: <i>Hypericum perforatum</i> L. Known as: Perforate St John's-wort, common Saint John's wort and simply St John's wort Herbal family: Hypericaceae	Digoxin	<i>Hypericum perforatum</i> reduces the therapeutic effect of digoxin and reduces the sub-curved level of digoxin.	[14-17]
	Nitrates	Reduce its sublingual absorption	[18]
	Anesthetics	Delay and prolong the effect of the drug	[17]
	Narcotic	Increase sleep time and sedative effect of the drug	[16,17]
	Piroxicam, Tetracyclines, Sulfonamides, Chlorpromazine, Thiazides	Increased sensitivity to light	[14-16]
	Theophylline	Exacerbation of asthma symptoms and decreased serum levels of the drug through induction of the Cyp450 system	[14,19]
	Warfarin	Increase the dose of the drug by reducing the effectiveness of the drug	[17]
	Iron	Inhibition of iron absorption due to the presence of tannic acid in the plant	[17,19]
	Estrogen	Uterine bleeding and reduced fertility	[14,17]
	Cyclosporine	Decreased serum levels of the drug through induction of the Cyp450 system	[15,12]
	Pseudoephedrine	Intensify the effect of the drug	[9]
	Indinavir	Decreased serum levels of the drug through induction of the Cyp450 system	[17,20]
	Antidepressants	Interaction of <i>Hypericum perforatum</i> with antidepressants can increase serotonin levels and cause serotonin syndrome.	[21]
	Ranolazine	This medicine should not be taken with ranolazine heart medicine	[22]

Table 2. Chemical Structure of bioactive compounds of *Hypericum perforatum*

Name	Chemical Structure
Epigallocatechin	 <p>The structure shows a flavan-3-ol core (epigallocatechin) consisting of a chromane ring system with a catechol group at position 2 and a gallic acid moiety at position 3. The gallic acid moiety is a benzene ring with three hydroxyl groups at positions 2, 3, and 4.</p>
Rutin	 <p>The structure shows a flavonol core (quercetin) with a rutinoside moiety at position 3. The rutinoside moiety consists of a glucose molecule linked to a rhamnose molecule via an ether bridge. The glucose molecule has hydroxyl groups at positions 2, 3, and 6, and a methyl group at position 4. The rhamnose molecule has hydroxyl groups at positions 2, 3, and 6.</p>
Hyperoside	 <p>The structure shows a flavonol core (quercetin) with a galactoside moiety at position 3. The galactoside moiety consists of a galactose molecule linked to the quercetin core via an ether bridge. The galactose molecule has hydroxyl groups at positions 2, 3, and 6.</p>
Iso quercetin	 <p>The structure shows a flavonol core (quercetin) with a galactoside moiety at position 3. The galactoside moiety consists of a galactose molecule linked to the quercetin core via an ether bridge. The galactose molecule has hydroxyl groups at positions 2, 3, and 6.</p>
Quercetin	 <p>The structure shows a flavonol core (quercetin) consisting of a chromone ring system with hydroxyl groups at positions 3, 5, 7, and 8, and a catechol group at position 2.</p>
Amento flavone	 <p>The structure shows a flavone core (amentoflavone) consisting of a chromone ring system with hydroxyl groups at positions 3, 5, 7, and 8, and a catechol group at position 2. It also features a p-coumaroyl moiety at position 6.</p>

Discussion

Studies have shown that *Hypericum perforatum* interferes with cardiac drugs, anesthetics, narcotics and analgesics, antibiotics, hormonal compounds, antiviral compounds, anticonvulsants and antidepressants, effective compounds Organ transplants and iron compounds. Despite the medicinal effects of the valuable plant *Hypericum perforatum*, the single use of this plant is very effective and valuable in the treatment of diseases and disorders, but its use with other chemical drugs due to the occurrence of drug interactions requires caution in use. Studies have shown that medicinal plants due to their active ingredients and medicinal and antioxidant compounds have beneficial effects on human health and have a therapeutic effect on various organs of the body and various diseases [23-33].

Consent for Publication: Not applicable.

Conflict of Interest: Such as receiving funds or fees by, or holding stocks and shares in, an organization that may profit or lose through publication of the paper.

Acknowledgements: Should be presented at the end of the paper and appropriately thanked the partners or sponsors. Also authors must declare any sources of funding.

References

- [1] Crompton CW, Hall IV, Jensen KIN and Hildebrand P. The biology of Canadian weeds. *Hypericum Perforatum* L. *Canadian J Plant Sci.* **1988**; 68: 149- 162.
- [2] Sirvent TM, Walker L, Vance N and Gibson DM. Variation in hypericins from wild populations of *Hypericum perforatum* L. In the Pacific Northwest of the U.S.A. *Economic Botany.* **2002**; 56: 41- 48.
- [3] Schulz V, Hansel R and Tyler VE. Rational phytotherapy. Springer- Verlag. Berlin Heidelberg. **1998**.
- [4] Campbell MH, May CE, Southwell IA, Tomlinson JD and Michael PW. Variation in *Hypericum Perforatum* L. (St. John's wort) in New South Wales. *Plant Protection Quaterly.* **1997**; 12: 64- 66.
- [5] Hobbs CH. St. John's wort. St John's wort. *Herbalgram.* **1996**; 35: 18-32.
- [6] Gerard J. The Herbal. Revised and enlarged by T. Johnson. reprint by Dover publications In: Hobbs Ch. St John's wort. *Herbalgram.* **1996**; 35: 18-32.
- [7] Campbell MH. Germination, emergence and seedling growth of *Hypericum perforatum* L. *Weed Res.* **1985**; 25: 259-266.
- [8] Umek A, Kreft S, Kartnig T, Heydel B. Quantitative phytochemical analyses of six hypericum species growing in slovenia". *Planta Med.* **1999**; 65 (4): 388–90.
- [9] Tatsis EC, Boeren S, Exarchou V, Troganis AN, Vervoort J, Gerothanassis IP. "Identification of the major constituents of *Hypericum perforatum* by LC/SPE/NMR and/or LC/MS". *Phytochem.* **2007**; 68 (3): 383–93.
- [10] Schwob I, Bessière JM, Viano J. Composition of the essential oils of *Hypericum perforatum* L. from southeastern France. *C R Biol.* **2002**; 325:781-5.
- [11] Sirvent TM, Walker L, Vance N, Gibson DM. Variation in hypericins from wild populations of *Hypericum perforatum* L. In the Pacific Northwest of the U.S.A. *Economic Botany.* **2002**; 56: 41- 48.
- [12] Barnes J, Anderson A, Phillipson D. St. John's wort (*Hypericum perforatum* L.): A review of its chemistry, pharmacology and clinical properties. *Journal of pharmacy and pharmacology.* 2001; 53: 583-600.
- [13] Baselt R. Disposition of Toxic Drugs and Chemicals in Man, 8th edition, Biomedical Publications, Foster City, CA, 2008, pp. 1445–1446.
- [14] Kuhn MA. Herbal Remedies: Drug – Herb Interactions. *Critical Care Nurse.* 2002; 22: 22- 32
- [15] Fleming T. PDR for Herbal Medicine. Second Edition; Medical economics Co. Montvale New Jersey, 2000
- [16] Brent J. Herbal drug interaction chart. <http://www.sdh.sk.ca/rxfiles>. July 2002.
- [17] Corponter DO. Nursing herbal medicine Handbook. springhouse corporation, springhouse. Pennsylvania; 2001; pp: 483 - 8.
- [18] Mills S, Bone K. Principle and practice of phytotherapy (Modern herbal medicine). Churchill Livingstone, 2000; pp: 104- 7.
- [19] Shih RD. Rosens Emergency Medicine: Concepts and Clinical Practice, 5th ed, Mosby, Inc. 2002; p: 2204.

- [20] <http://www.vitalgoods.com/myibis/herbdrug.pdf>.
- [21] Borrelli F, Izzo AA. Herb-drug interactions with St John's wort (*Hypericum perforatum*): an update on clinical observations. *AAPS Journal*. 2009; 11 (4): 710–27.
- [22] Renolazine. MedlinePlus, US National Library of Medicine. 15 January 2016. Retrieved 21 June 2017.
- [23] Moayeri A, Azimi M, Karimi E, Aidy A, Abbasi N. Attenuation of Morphine Withdrawal Syndrome by Prosopis Farcta Extract and Its Bioactive Component Luteolin in Comparison with Clonidine in Rats. *Med Sci Monitor Basic Res* 2018; 24(9): 151-158.
- [24] Bahmani M, Taherikalani M, Khaksarian M, Rafeian-Kopaei M, Ashrafi B, Nazer M, Soroush S, Abbasi N, Rashidipour M. The synergistic effect of hydroalcoholic extracts of Origanum vulgare, Hypericum perforatum and their active components carvacrol and hypericin against Staphylococcus aureus. *Future Science OA* 2019; 5(3): Article number FSO371.
- [25] Abbasi N, Khosravi A, Aidy A, Shafiei M. Biphasic response to luteolin in MG-63 osteoblast-like cells under high glucose-induced oxidative stress. *Iranian Journal of Medical Sciences* 2016; 41(2): 118-125.
- [26] Bahmani M, Taherikalani M, Khaksarian M, Rafeian-Kopaei M, Ashrafi B, Nazer M, Soroush S, Abbasi N, Rashidipour M. The synergistic effect of hydroalcoholic extracts of Origanum vulgare, Hypericum perforatum and their active components carvacrol and hypericin against Staphylococcus aureus. *Future Science OA* 2019; 5(3): Article number FSO371.
- [27] Zangeneh MM, Ghaneialvar H, Akbaribazm M, Ghanimatdan M, Abbasi N, Goorani S, Pirabbasi E, Zangeneh A. Novel synthesis of Falcaria vulgaris leaf extract conjugated copper nanoparticles with potent cytotoxicity, antioxidant, antifungal, antibacterial, and cutaneous wound healing activities under in vitro and in vivo condition. *Journal of Photochemistry and Photobiology B: Biology* 2019; 197, art. no. 111556, .
- [28] Mahdavi B, Saneei S, Qorbani M, Zhaleh M, Zangeneh A, Zangeneh MM, Pirabbasi E, Abbasi N, Ghaneialvar H. Ziziphora clinopodioides Lam leaves aqueous extract mediated synthesis of zinc nanoparticles and their antibacterial, antifungal, cytotoxicity, antioxidant, and cutaneous wound healing properties under in vitro and in vivo conditions. *Applied Organometallic Chemistry* 2019; 33 (11), art. no. e5164.
- [29] Valadi A, Nasri S, Abbasi N, Amin GR. Antinociceptive and anti-inflammatory effects of hydroalcoholic extract of Anethum graveolens L. seed. *Journal of Medicinal Plants* 2010; 9(34):124-130.
- [30] Alizadeh M, Safarzadeh A, Bahmani M, Beyranvand F, Rafeian-Kopaei M, Abbaszadeh S. Brucellosis: Pathophysiology and new promising treatments with medicinal plants and natural antioxidants. *Asian Pacific J Trop Med* 2018; 11(11): 597-608.
- [31] Abbaszadeh S, Andevvari AN, Koohpayeh A, Naghdi N, Alizadeh M, Beyranvand F, Harsej Z. Folklore medicinal plants used in liver disease: A review. *Int J Green Pharmacy* 2018; 12(3): 463-472.
- [32] Sedighi M, Sewell R.D.E, Nazari A, Abbaszadeh S, Cheraghi M, Amini A, Heydari Z, Rafeian-Kopaei M. A review on the most important medicinal plants effective in cardiac ischemia-reperfusion injury. *Current Pharmaceutical Design* 2019; 25(3): 352-358.
- [33] Eftekhari Z. Antimicrobial properties of medicinal plants; The new therapeutic aspect of Valeriana officinalis. *Plant Biotechnol Persa*. 2020; 2 (1) :59-60
- [34] F. Magbool F, Ibrahim Elnima E, M. E S, I. Hamedelniei E, Mahmoud Gamil A, E. Adam M et al. FORMULATION DESIGN, DEVELOPMENT AND EVALUATION OF QUERCUS INFECTORIA GALLS EXTRACT ORAL GELS. *Plant Biotechnol Persa*. 2020; 2 (2): 1-13.
- [35] Nouri A, Heidarian E, Amini-Khoei H, Abbaszadeh S, Basati G. Quercetin through mitigation of inflammatory response and oxidative stress exerts protective effects in rat model of diclofenac-induced liver toxicity. *J Pharmacy Pharmacog Res* 7(3): 2019, Pages 200-212.