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Bibliografía: Hypericum Perforatum: propiedades analíticas, formas farmacéuticas, dosis, estabilidad, propiedades físicas, químicas.

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Stable extract of hypericum perforatum L. process for preparing it and pharmaceutical compositions containing the extracts / Clemens Erdelmeier; Eckhaut Grethkin; Friedrich Lang (et.al).-- **PCT Int. Appl. WO 97 13,489** 17 Apr. 1997 14p.--(al) *** C.A. 126:334371n

St.Jhon´s wort as antidepressant / Klaus F. Rammert.-- Dtsch.Apoth.Ztg. 136(46): 4131-4132,1996 (Al) C.A. 126:139298s ***

Phytopharmaceuticals in old age. Crataegus, ginkgo, hypericum, and kava-kava preparations / Theo Dingermann.-- Pharm. Ztg. 140(23):9-14,16,1995 (Al) C.A. 124:15314h ***

Hypericum perforatum / Ezio Bombardelli; Paolo Morazzoni.-- Fitoterapia 66(1):43-68,1995 C.A. 123:222694b ***

Application of information theory and numerical taxonomy methods to thin layer chromatographic investigations of Hypericum Perforatum L / Marica Medic-Saric; Adelheid Brantner; Zeljan Males.-- Acta Pharm.(Zagreb) 46(2):115-124,1996 C.A. 125:123858t análisis

Hypericum perforatum as source of drugs used in treating depression / Anon.-- Herba Pol. 42(3):192-98,1996 (Pol) C.A. 125:315998k

Pharmacological study of the antidepressive effect of Hypericum Perforatum L. / H. Winterhoff; V. Butterweck; A. Nahrsted; H.G. Gumbinger (et.al).-- Phytopharmaka Forsch.Klin.Anwend. p.39-56,1995 (Al)Steinkpff: Darmstadt, ed. Dieter Loew; Norbert Rietbrock C.A. 125:26140v

Comparative phytochemical investigations of Hypericum Perforatum L. and Hypericum maculatum Crantz / A. Brantner; T. Kartnig; F. Quehenberger.-- Sci.Pharm. 62(3):261-76,1994 (Al) C.A. 122:3106441s

Phenolic compounds from Hypericum Perforatum and H. undulatum / Rosa M. Seabra; M. Helena Vasconcelos; M.A. Cruz Costa (et.al).-- Fitoterapia 63(5):473-4,1992 (ingl) C.A. 118: 165204n

Hypericin content variation in Hypericum perforatum in Australia / Ian A. southwell; Malcolm H. Campbell.-- Phytochemistry 30(2): 475-8,1991 C.A. 114:118562k

St. John´s wort (Hypericum Perforatum L.) Genotoxicity due to the quercetin content / Barbara Poginski; Johannes Westendorf; Nikolaya Prosenc (et.al).-- Dtsch. Apoth.Ztg. 128(26):1364-6,1988 (Al) C.A. 109:183514g

St. John´s wort (Hypericum Perforatum L.) HPLC analysis of the main components and their variability in a population / Josef Hoelzl; Elke Ostrowski.-- Dtsch.Apoth.Ztg. 127(23): 1227-30,1987 (Al) C.A. 107:112686n

Thin-layer chromatography of extracts of Hypericum perforatum / A. Stoyanova; M. Popova; E. Georgiev.-- Farmatsiya (Sofía) (1): 8-13,1987 (Búlg) C.A. 107:205272q

Experimental animal studies of the psychotropic activity of a Hypericum extract / S.N. Okpanyi; M.L. Weischer.-- Arzneim. Forsch. 37(1):10-13,1987 (Al) C.A. 106:113450x

Effect of solvent and moisture of St.- Jhon´s wort on extraction of some biologically active substances.II. Extraction of hypericin with glycol / E. Georgiev; M. Popova; A. Stoyanova.-- **Nauchi Tr. Vissh Inst.**

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Khranit. Vkusova Prom-st Plovdiv 32(1).257-63,1985 c.A. 105:29872

Determination of flavonoides in Hypericum Perforatum / I. Dorosiev.-- Pharmazie 40(8):585-6, 1985 (Ingl) C.A. 104:3434w

Pharmacopsychiatry 1997 Sep;30 Suppl 2:129-134

Biologically active and other chemical constituents of the herb of Hypericum perforatum L.

Nahrstedt A, Butterweck V

Department of Pharmaceutical Biology and Phytochemistry, Westphalian Wilhelms University of Munster, Germany.

Phenylpropanes, flavonol derivatives, biflavones, proanthocyanidins, xanthones, phloroglucinols, some amino acids, naphthodianthrones and essential oil constituents are the natural plant products known from the crude drug of Hypericum perforatum, Hyperici herba. These compounds are discussed with respect to structural features, their concentration, biological activities and their possible contribution to the clinically demonstrated antidepressant efficacy of extracts obtained from Hyperici herba. Publication Types: Review

Pharmacopsychiatry 1997 Sep;30 Suppl 2:125-128

Testing the antidepressant effects of Hypericum species on animal models.

Ozturk Y

Medicinal and Aromatic Plant and Drug Research Centre, Anadolu University, Eskisehir, Turkey.

This paper summarizes the antidepressant effects of certain Hypericum species on animal models. Although there are many drugs in clinical use for the management of human depression, most of the antidepressant drugs have undesirable side effects, some of which may limit the daily life of patients, and therefore, more specific agents with lesser side effects are necessary as a new therapeutic modality for the rational treatment of depression. In our laboratory, we observed antidepressant activity with the alcoholic extract of H. calycinum whose effects on the central nervous system of mice are almost equal to the extract prepared from St. John's wort, H. perforatum. Other species, H. hyssopifolium ssp. elongatum var. elongatum seems to have no antidepressant activity. From these data, it can be concluded that at least some of Hypericum species may have a potential use for the treatment of depression. Publication Types: Review

Pharmacopsychiatry 1997 Sep;30 Suppl 2:117-124

Effects of the total extract and fractions of Hypericum perforatum in animal assays for antidepressant activity.

Butterweck V, Wall A, Lieflander-Wulf U, Winterhoff H, Nahrstedt A

Department of Pharmacology and Toxicology of the Westphalian Wilhelms University of Munster, Germany.

A commercially available extract of the aerial parts of Hypericum perforatum, LI 160, showed pronounced activity in selected animal bioassays. These include the forced swimming test (FST) and the tail suspension test, used to determine antidepressant activity, and tests indicating activity on the central nervous system, such as body temperature and ketamine induced sleeping time. The counteracting effects of drugs known to interfere with the central dopaminergic system strongly suggested that

dopamine mediated activity is important for the activity of the extract. Dose-response experiments of the total extract and of
fractions rich in flavonoids and napthodianthrones produced inverted U-shaped dose response curves.

Pharmacopsychiatry 1997 Sep;30 Suppl 2:113-116

Effects of long-term administration of hypericum extracts on the affinity and density of the central serotonergic 5-HT1 A and 5-HT2 A receptors.

Teufel-Mayer R, Gleitz J

Department of Naturheilkunde, Ulm University, Germany.

Extracts of St. John's wort, Hypericum perforatum L. (Hypericaceae), are used as a phytotherapeutic antidepressant. A
number of clinical studies demonstrate that their antidepressive potency is comparable to tricyclic antidepressants (TCA).
Although the therapeutic effect of hypericum extracts is well documented, very little is known about the molecular mode of
action. As the improvement of the depressive symptoms with both TCA and hypericum extracts only occurs significantly after a
lag phase of 10 to 14 days, it is assumed that the medication causes long-term adaptations within the central nervous system. In
this context, serotonergic (5-HT) receptors are of special interest. Therefore, we investigated possible alterations in affinity and
density of 5-HT1 A and 5-HT2 A receptors caused by long-term treatment of rats with St. John's wort. The brain without
cerebellum and brain stem of rats, treated daily for 26 weeks with a commercially available hypericum extract (2700 mg/kg LI
160) were used for membrane preparations. Affinity (KD) and amount (Bmax) of serotonergic receptors were determined by
employing receptor binding assays using 3 H-8-OH-DPAT and 3H-Ketanserin as selective radioligands for the 5-HT1 A and
the 5-HT2 A receptors, respectively. We found that in hypericum-treated rats the number of both 5-HT1 A and 5-HT2 A
receptors were significantly increased by 50% compared to controls, whereas the affinity of both serotonergic receptors
remained unaltered. The data suggest an upregulation of 5-HT1 A and 5-HT2 A receptors due to prolonged administration of
hypericum extracts. These results are consistent with a modification of the expression levels of serotonergic receptors caused
by synthetic antidepressants.

Pharmacopsychiatry 1997 Sep;30 Suppl 2:108-112

In vitro receptor binding and enzyme inhibition by Hypericum perforatum extract.

Cott JM

Pharmacologic Treatment Research Program, National Institute of Mental Health (NIMH), National Institutes of Health,
Rockville, Maryland, USA.

Hypericum perforatum L. Hypericaceae (St. John's wort), has been used since the time of ancient Greece for its many
medicinal properties. Modern usage is still quite diverse and includes wound healing, kidney and lung ailments, insomnia and
depression. This plant has been known to contain a red pigment, hypericin, and similar compounds, which have been assumed
to be the primary active constituent(s) in this plant genus. A crude Hypericum extract was tested in a battery of 39 in vitro
receptor assays, and two enzyme assays. A sample of pure hypericin was also tested. Hypericin had affinity only for NMDA
receptors while the crude extract had significant receptor affinity for adenosine (nonspecific), GABAA, GABAB,

benzodiazepine, inositol triphosphate, and monoamine oxidase (MAO) A and B. With the exception of GABAA and GABAB,
the concentrations of Hypericum exact required for these in vitro activities are unlikely to be attained after oral administration in
whole animals or humans. These data are consistent with recent pharmacologic evidence suggesting that other constituents of
this plant may be of greater importance for the reported psychotherapeutic activity. Alternative pharmacologic mechanisms for
Hypericum's antidepressant activity are critically reviewed and the possible importance of GABA receptor binding in the
pharmacology of Hypericum is highlighted. Some of these results have been previously reported.

Pharmacopsychiatry 1997 Sep;30 Suppl 2:94-101

Hypericin and pseudohypericin: pharmacokinetics and effects on photosensitivity in humans.

Brockmoller J, Reum T, Bauer S, Kerb R, Hubner WD, Roots I

Department of Clinical Pharmacology of the Charite, Humboldt University of Berlin, Germany.

Extracts of St. John's wort (Hypericum perforatum) are used in treatment of depression. They contain various substances with
the naphthodianthrones hypericin and pseudohypericin as characteristic ingredients. These compounds were shown to cause
phototoxicity in cell culture and in animals. A placebo-controlled randomized clinical trial with monitoring of hypericin and
pseudohypericin plasma concentration was performed to evaluate the increase in dermal photosensitivity in humans after
application of high dose hypericum extracts. The study was divided into a single dose and a multiple dose part. In the single
dose period, each of 13 volunteers received in a double blind fourfold complete crossover design, either placebo, or 900, 1800
or 3600 mg of a standardized hypericum extract (LI 160) containing zero, 2.81, 5.62 and 11.25 mg of total hypericin (total
hypericin is the sum of hypericin and pseudohypericin). Maximum total hypericin plasma concentrations were observed about 4
h after dosage and were 0, 0.028, 0.061 and 0.159 mg/L, respectively. Before and 4 h after drug intake, the subjects were
exposed at small areas of their back to increasing doses of solar simulated irradiation (SSI, with combined ultraviolet A, UV-A,
and UV-B light) and another part was exposed to selective UV-A light irradiation. Minimal erythema dose was determined 5,
20 and 68 h after irradiation. Comparison of SSI sensitivity without and with hypericum extract did not show and difference
and there was no dose-related trend in light sensitivity. Sensitivity to selective UV-A light was increased only after the highest
dose from a minimal tanning dose of 10.8 J/ cm2 (mean) after placebo to 8.7 J/cm2 after 3600 mg extract with marginal
statistical significance ($p = 0.03$ by one sided paired t-test). There was no correlation between total hypericin plasma
concentrations and photosensitivity. In the multiple dose part, 50 volunteers received 600 mg hypericum extract t.i.d. with a
daily dose of 5.6 mg of total hypericin. Comparison of UV light sensitivity before dosing with day 15 of treatment showed a
slightly increased SSI sensitivity expressed by decrease of the MED from 0.17 to 0.16 J/cm2 ($p = 0.005$ by Wilcoxon test),
and similarly, sensitivity to UV-A light increased (the mean tanning dose decreased from 9.9 to 7.8 J/cm2, $p < 0.0001$). This
increase in cutaneous light sensitivity could be compensated by reducing irradiation time by 21%. Doses used in this study were
higher than typical doses in current commercial preparations. In spite of these high doses in the double blind single dose part,
frequency of side effects was equal to placebo medication and UV light sensitivity was not or only marginally increased. The
study does not, however, exclude phototoxic reactions with doses above 11.25 mg of total hypericin and

plasma levels above
100 micrograms/L. Furthermore, phototoxicity may be different after application of pure hypericin, since some constituents in
the plant extract may exhibit protective effects. Publication Types:Clinical trial

J Chromatogr B Biomed Sci Appl 1997 Aug 1;695(2):309-316

Determination of naphthodianthrones in plant extracts from Hypericum perforatum L. by liquid chromatography-electrospray mass spectrometry.

Piperopoulos G, Lotz R, Wixforth A, Schmierer T, Zeller KP

Eberhard-Karls-Universitat, Institut fur Organische Chemie, Tubingen, Germany.

The determination of the naphthodianthrone constituents in extracts of dried blossoms of Hypericum perforatum L. by
combined HPLC-electrospray mass spectrometry is described. Hypericin (1), pseudohypericin (2) and their precursor
compounds produce intensive negative quasi-molecular ions by deprotonation provided a non-acidic eluent system is used in
the HPLC separation. From the [M-H]- ions formed in the electrospray ionization process characteristic daughter ion spectra
can be obtained by collisional activation which have been studied by tandem mass spectrometry.

Lakartidningen 1997 Jun 18;94(25):2365-2367

[St John's wort against depression in favour again].

[Article in Swedish]

Nordfors M, Hartvig P

Sodra Stockholms sjukvardsomrade.

Extracts of Hypericum perforatum St. John's wort, have been used since antiquity for the treatment of depressive symptoms. In
25 controlled clinical trials where hypericum extract was compared with placebo and established antidepressants, improvement
was obtained in 61 percent of patients on low-dose treatment (< 1.2 mg hypericum extract), and in 75 percent of patients
treated with a higher dose (2.7 mg). The side effects were mild and occurred at lower frequency than did those of other
antidepressants. The constituent of hypericum extract that is responsible for the antidepressant effect has not been identified.
Nor is the mechanism of action known, but a combination of low-grade monoamine oxidase inhibition and noradrenaline and
serotonin reuptake blockade seems the most likely alternative, though other interesting mechanisms have also been proposed.
Owing to their beneficial effect and low toxicity, preparations containing extracts from H perforatum might furnish an alternative
to established therapy, especially among patients concerned about stigmatization or less apprehensive of herbal medication than of synthetic drugs. Publication Types: Review

Pharm Acta Helv 1997 Jun;72(3):153-157

Inhibition of benzodiazepine binding in vitro by amentoflavone, a constituent of various species of Hypericum.

Baureithel KH, Buter KB, Engesser A, Burkard W, Schaffner W

Dept. of Pharmaceutical Biology, University of Basel, Switzerland.

Flower extracts of Hypericum perforatum, Hypericum hirsutum, Hypericum patulum and Hypericum olympicum efficiently

inhibited binding of [3H]flumazenil to rat brain benzodiazepine binding sites of the GABAA-receptor in vitro with IC50 values
of 6.83, 6.97, 13.2 and 6.14 micrograms/ml, respectively. Single constituents of the extracts like hypericin, the flavones
quercetin and luteolin, the glycosylated flavonoides rutin, hyperoside and quercitrin and the biflavone 13, II8-biapigenin did not
inhibit binding up to concentrations of 1 microM. In contrast, amentoflavone revealed an IC50 = 14.9 +/- 1.9 nM on
benzodiazepine binding in vitro. Comparative HPLC analyses of hypericin and amentoflavone in extracts of different Hypericum
species revealed a possible correlation between the amentoflavone concentration and the inhibition of flumazenil binding. For
hypericin no such correlation was observed. Our experimental data demonstrate that amentoflavone, in contrast to hypericin,
presents a very active compound with regard to the inhibition of [3H]-flumazenil binding in vitro and thus might be involved in
the antidepressant effects of Hypericum perforatum extracts.

Nervenarzt 1997 Feb;68(2 Suppl):8

[Hypericum perforatum in psychiatric practice].

[Article in German]

Kasper S

Nervenarzt 1997 Feb;68(2 Suppl):3-4

[Chemical composition of Hypericum perforatum and its effects].

[Article in German] ***

BMJ 1996 Aug 3;313(7052):253-258

St John's wort for depression--an overview and meta-analysis of
randomised clinical trials.

Linde K, Ramirez G, Mulrow CD, Pauls A, Weidenhammer W, Melchart D

Projekt Munchener Modell, Ludwig-Maximilians-Universitat, Munich, Germany.

OBJECTIVE--To investigate if extracts of Hypericum perforatum (St John's wort) are more effective than placebo in the
treatment of depression, are as effective as standard antidepressive treatment, and have fewer side effects than standard
antidepressant drugs. DESIGN--Systematic review and meta-analysis of trials revealed by searches. TRIALS--23 randomised
trials including a total of 1757 outpatients with mainly mild or moderately severe depressive disorders: 15 (14 testing single
preparations and one a combination with other plant extracts) were placebo controlled, and eight (six testing single preparations
and two combinations) compared hypericum with another drug treatment. MAIN OUTCOME MEASURES--A pooled
estimate of the responder rate ratio (responder rate in treatment group/responder rate in control group), and numbers of
patients reporting and dropping out for side effects. RESULTS--Hypericum extracts were significantly superior to placebo
(ratio = 2.67; 95% confidence interval 1.78 to 4.01) and similarly effective as standard antidepressants (single preparations
1.10; 0.93 to 1.31, combinations 1.52; 0.78 to 2.94). There were two (0.8%) drop outs for side effects with hypericum and
seven (3.0%) with standard antidepressant drugs. Side effects occurred in 50 (19.8%) patients on hypericum and 84 (52.8%)
patients on standard antidepressants. CONCLUSION--There is evidence that extracts of hypericum are more effective than
placebo for the treatment of mild to moderately severe depressive disorders. Further studies comparing

extracts with standard
antidepressants in well defined groups of patients and comparing different extracts and doses are needed.

Publication Types: Meta-analysis Comments: Comment in: BMJ 1996 Aug 3;313(7052):241-2
Comment in: BMJ 1996 Nov 9;313(7066):1204-5

Fortschr Med 1995 Sep 10;113(25):354-355

[St. John's wort as antidepressive therapy].

[Article in German]

Ernst E

Centre for Complementary Health Studies, Postgraduate Medical School, Exeter, UK.

St. John's Wort (Hypericum perforatum) has been used to treat a variety of complaints since ancient times. Recent studies have
shown that it is clinically effective for the treatment of the symptoms of depression. It has proved superior to placebo, equally as
effective as standard medication and has a clear advantage over the latter in terms of side-effects. It follows that, on the basis of
our present knowledge, St. John's Wort can be recommended for use as an anti-depressant.

Publication Types: Review

Psychopharmacol Bull 1995;31(4):745-751

NCDEU update. Natural product formulations available in europe for
psychotropic indications.

Cott J

Division of Clinical and Treatment Research, National Institute of Mental Health, Rockville, MD 20857, USA.

Until the middle of this century, development of medical treatment for human disease was intimately connected with the plant
kingdom. Despite advances of the last three decades in utilizing chemical synthetic approaches to drug design and sophisticated
structure-activity studies, there is still a great need for novel compounds with unique mechanisms of action in the field of
medicine. While many thousands of structural analogs have been synthesized and tested, numerous gaps remain in the
therapeutic armamentarium for psychiatric illnesses. Most new drugs marketed for psychotherapeutic indications in recent years
have been only incremental improvements on existing medications. Major breakthroughs have resulted primarily from the study
of natural products. Some of our most valuable drugs have been isolated from plant and animal sources, including aspirin,
morphine, reserpine (the first antipsychotic), almost all of our antibiotics, digitalis, and such anti-cancer agents as vincristine,
vinblastine, and taxol. Recent political and social events suggest that new emphasis will be placed on natural products research
in the years to come. This article highlights therapeutic applications of Ginkgo biloba, Hypericum perforatum, Valerian
officinalis, and Panex ginseng. Publication Types: Review

J Geriatr Psychiatry Neurol 1994 Oct;7 Suppl 1:S47-S53

Pharmacokinetics of hypericin and pseudohypericin after oral intake of
the hypericum perforatum extract LI 160 in healthy volunteers.

Staffeldt B, Kerb R, Brockmoller J, Ploch M, Roots I

Institut fur Klinische Pharmakologie, Universitatsklinikum Charite Berlin, Germany.

The single- and multiple-dose pharmacokinetics of the naphthodianthrones hypericin and pseudohypericin derived from St.
John's wort (Hypericum perforatum, LI 160, Lichtwer Pharma GmbH, Berlin) were studied in 12 healthy male subjects. After a
single oral dose of 300, 900, or 1800 mg of dried hypericum extract (250, 750, or 1500 micrograms hypericin and 526, 1578,
or 3156 micrograms pseudohypericin), plasma levels were measured with a modified highly sensitive high-pressure liquid
chromatography (HPLC) method (lower detection limit 0.1 ng/mL) up to 3 days. The median maximal plasma levels were 1.5,
4.1, and 14.2 ng/mL for hypericin and 2.7, 11.7, and 30.6 ng/mL for pseudohypericin, respectively, for the three doses given
above (interim evaluation of four volunteers). The median elimination half-life times of hypericin were 24.8 to 26.5 hours, and
varied for pseudohypericin from 16.3 to 36.0 hours. Ranging between 2.0 to 2.6 hours, the median lag-time of absorption was
remarkably prolonged for hypericin when compared to pseudohypericin (0.3 to 1.1 hours). The areas under the curves (AUC)
showed a nonlinear increase with raising dose; this effect was statistically significant for hypericin. During long-term dosing (3 x
300 mg/day), a steady-state was reached after 4 days. Mean maximal plasma level during the steady-state treatment was 8.5
ng/mL for hypericin and 5.8 ng/mL for pseudohypericin, while mean trough levels were 5.3 ng/mL for hypericin and 3.7 ng/mL
for pseudohypericin. In spite of their structural similarities there are substantial pharmacokinetic differences between hypericin
and pseudohypericin. Publication Types: Clinical trial

Vet Hum Toxicol 1993 Aug;35(4):298-300

Studies of sheep experimentally poisoned with Hypericum perforatum.

Kako MD, al-Sultan II, Saleem AN

Department of Pathology, College of Veterinary Medicine, University of Mosul, Iraq.

Sheep given different dosages and frequencies of Hypericum perforatum had decreased hemoglobin, red blood cell count,
packed cell volumes, total protein, glucose, cholesterol, triglycerides, and serum alkaline phosphotase activities. Blood urea
nitrogen, sodium, potassium, bilrubin (total and direct), and the activities of aspartate aminotransferase, alanine
aminotransferase, lactate dehydrogenase and gamma glutamyltransferase increased. Hemato-biochemical assays were useful
diagnostic aids to determine the severity of this plant's toxic effects.

Nauchnye Doki Vyss Shkoly Biol Nauki 1992;4:9-13

[The modification of a radiation lesion in animals with an aqueous extract
of Hypericum perforatum L. 2].

[Article in Russian]

Smyshliaeva AV, Nguyen LH, Kudriashov IuB

The preparation Hypericum perforatum L. has been shown to decrease the intensity level of enzymatic and non-enzymatic
processes of lipid peroxidation of rat liver microsomes in vitro and in vivo. In the mucus of the this intestine in vivo the increase
of the number of non-enzymatic SH-groups is observed. Possible mechanisms of radioprotective action of the preparation is under discussion.

Arzneimittelforschung 1991 May;41(5):481-483

Vasoactive properties of procyanidins from Hypericum perforatum L. in

isolated porcine coronary arteries.

Melzer R, Fricke U, Holzl J

Institut fur Pharmazeutische Biologie Universitat Marburg, Marburg/Lahn, Fed. Rep. of Germany.

Procanidin fractions (PC) were isolated from Hypericum perforatum L. (Guttiferae). Characterization of the main components
of each fraction was performed by UV- and mass spectroscopy. Their biological activity was tested in porcine isolated
coronary arteries. All PC fractions antagonized histamine- or prostaglandin F2 alpha-induced arterial contractions. In contrast,
vasorelaxation was insignificant in KCl-precontracted coronary arteries except with the higher oligomeric PC fraction 3.
Vasoactive properties of the PC seem to be dependent on their relative molecular mass. An inhibition of cellular
phosphodiesterase might be involved in the underlying mechanism of action.

Arzneimittelforschung 1990 Aug;40(8):851-855

[Genotoxicity of a standardized Hypericum extract].

[Article in German] ***

Okpanyi SN, Lidzba H, Scholl BC, Miltenburger HG

Steigerwald Arzneimittelwerk GmbH, Darmstadt.

St. John's wort (Hypercum perforatum) contains hypericin and hypericin-like substances as well as flavonoids, of which
particularly Quercetin has generated a wide-spread controversial discussion with respect to mutagenic action. The genotoxicity
of a standardized aqueous ethanolic Hypericum extract (Hypericum extract Steigerwald, Psychotonin M) was verified in
different in-vivo and in-vitro testsystems with mammalian cells. The in-vitro investigations were performed with the HGPRT
(hypoxanthine guanidine phosphoribosyl transferase)-test, UDS (unscheduled DNA synthesis)-test and with the cell
transformation test using Syrian hamster embryo cells. Both the in-vitro tests as well as the in-vivo tests--fur spot test of the
mouse and the chromosome aberration test with the bone marrow cells of the chinese hamster--were negative, giving
completely no indication of a mutagenic potential of Hypericum extract. These investigations lend support to the view that
results from bacterial short-term tests are of very limited transferability to human.

Tierarztl Prax 1989;17(3):257-261

[Hypericum poisoning in sheep].

[Article in German]

Kumper H

Medizinischen und Gerichtlichen Veterinarklinik II, Justus-Liebig-Universitat Giessen.

A report about a case of St. John's wort poisoning in German Blackface sheep is given. After the ingestion of St. John's wort
(Hypericum perforatum) all slightly pigmented parts of the skin, that were rarely covered with hair, were photosensitized. In
summer many sheep suffered from inflammatory skin alterations at the ears, the bridge of the nose and at the surroundings of
the eyes. A literature review informs about etiology and treatment of photosensitivity disease and the St. John's wort is exactly

described to facilitate recognition.

Arzneimittelforschung 1987 Jan;37(1):10-13

[Animal experiments on the psychotropic action of a Hypericum extract].

[Article in German]

Okpanyi SN, Weischer ML

Extracts of Hypericum perforatum (Psychotonin M) (St. John's wort) with known concentrations of hypericin were tested in
several models generally accepted as screening methods in experimental animal studies for the recognition of psychotropic, and
in particular of antidepressant activity. Hypericum extract enhanced the exploratory activity of mice in a foreign environment,
significantly prolonged the narcotic sleeping time dose-dependently, and within a narrow dose range exhibited reserpine
antagonism. Similar to most other antidepressants, hypericum extract enhanced significantly the activity of mice in the water
wheel test and after a prolonged daily administration decreased aggressiveness in socially isolated male mice. The presented
data in addition to the already proven clinical efficacy justify the use of standardised Hypericum extract in the treatment of mild to moderate depression.

Toxicol Lett 1982 Feb;10(2-3):183-188

Consumption of poisonous plants (Senecio jacobaea, Symphytum officinale,
Pteridium aquilinum, Hypericum perforatum) by rats: chronic toxicity,
mineral metabolism, and hepatic drug-metabolizing enzymes.

Garrett BJ, Cheeke PR, Miranda CL, Goeger DE, Buhler DR

Effect of dietary tancy ragwort (Senecio jacobaea), comfrey (Symphytum officinale), bracken (Pteridium aquilinum) and alfalfa
(Medicago sativa) on hepatic drug-metabolizing enzymes in rats were measured. Tansy ragwort and bracken increased (P less
than 0.05) the activity of glutathione transferase and epoxide hydrolase. Comfrey and alfalfa increased (P less than 0.05) the
activity of aminopyrine N-demethylase. Feeding bracken or St. John's wort (Hypericum perforatum) in conjunction with tansy
ragwort did not influence chronic toxicity of tansy ragwort as assessed by rat survival time. Dietary tansy ragwort resulted in
increased (P less than 0.05) hepatic copper levels; the other plants did not affect copper levels. The results do not suggest any
major interaction in the toxicity of tansy ragwort with bracken or St. John's wort.

J Comp Pathol 1981 Jan;91(1):135-141

An investigation of the type of photosensitization caused by the ingestion of
St John's Wort (Hypericum perforatum) by calves.

Araya OS, Ford EJ

Rev Med Chir Soc Med Nat Iasi 1977 Jan;81(1):73-74

[Value of Hypericum perforatum oil in dermatological preparations. I].

[Article in Romanian]

Matei I, Gafitanu E, Dorneanu V

Vet Med Nauki 1981;18(6):87-94

[Anti-inflammatory action of a group of plant extracts].

[Article in Bulgarian]

Shipochliev T, Dimitrov A, Aleksandrova E

Use was made of Wistar albino rats in which an inflammation was induced via the simultaneous injection of caraginan and
prostaglandin E1 in order to evaluate the antiinflammatory activity of 6 freeze dried plant extracts. It was found that with such
model of inflammation the inflammatory effect of caraginan was strongly enhanced, which was accompanied by the rapid and
prolific white blood cell extravasates. The freeze-dried extracts of St. John's-wort (Hypericum perforatum L.), potmarigold
calendula (Calendula officinalis L.), camomile (Matricaria chamomilla L.) and plantain (Plantago lanceolata L. et Pl. major L.)
were found to suppress both the inflammatory effect and the leukocyte infiltration. The extracts of symphytum (Symphytum
officinale L.) and those of flax seed (Linum usitatissimum L.) did not inhibit the inflammation, however, they suppressed the
leukocyte infiltration at the 3rd and 4th hour of the induced inflammation.

Farm Zh 1973 Sep;28(5):92-93

[Growth sites of klamath seed (Hypericum perforatum L.) in Lvov Province and a determination of the quantity of extractable substances in the raw material].

[Article in Ukrainian]

El'iashevich OG

Antibiotiki 1971 Jun;16(6):510-513

[Antibiotic hyperforin from Hypericum perforatum L].

[Article in Russian]

Gurevich AI, Dobrynin VN, Kolosov MN, Popravko SA, Riabova ID

Antibiotiki 1977 Jul;22(7):630-634

[Effect of novoimanine on the cellular permeability indices of staphylococci].

[Article in Russian]

Avenirova EL

Novoimanine is an antibacterial drug from Hypericum perforatum L. When used in the bacteriostatic concentration, i.e. 0.5
gamma/ml, it induced release of potassium ions from the cells of Staphylococcus aureus 209P and had no effect on release of
the UV-absorbing compounds and 14C-amino acids. In addition, incubation of the cells with novoimanine (2.5--50 gamma/ml)
provided "preservation" in them of the earlier absorbed 14C-amino acids, while in the control cells their level decreased. In a
concentration of 100 gamma/ml novoimanine stimulated activity of ATP-ase and alkaline phosphatase by 34 and 37-57 per
cent respectively. Histones F1 and F3 of the calf thymus induced an intensive release of 14C-amino acids from the cells of
staphylococci and increased the activity of ATP-ase by 6-10 times. The data of the study suggested that the effect of
novoimanine on the cytoplasmic membrane was limited and different from that on the polycationic antibacterial agents.

Trivial Name: Hypericin
Synonym(s): 1,3,4,6,8,13-Hexahydroxy-10,11-dimethylphenanthro[1,10,9,8-*opqra*]perylene-7,14-dione, $_{9Cl}$. Mycoporphyrin. Hypericum red
Chapman & Hall Number: HJG16-U
CAS Registry Number: 548-04-9
Type of Compound Code(s): XA6600, XA2400, XA1450, VQ9000, VQ6000

Molecular Formula: $C_{30}H_{16}O_8$
Molecular Weight: M 504.452.
General Statement: The 7,14-dioxo tautomer (illus.) is the stable one. Several other tautomers have been obt. Numbering systems vary.
Source/Synthesis: Isol. from the mealy bug *Nipaecoccus aurilanatus*. Widespread in *Hypericum* spp. esp. *Hypericum perforatum* (St. John's wort) which is used as a folk remedy for treating depression and other nervous disturbances.
Use/Importance: Antidepressant, tranquilliser; shows potent antiretroviral activity.
Physical Description: Solvated blue-black needles.
Melting Point: Mp 300° dec..
Partition Coefficient: Log P 4.55 (calc).
Other Data: Yields cherry-red soln. with red fluor. in org. bases.
Supplier(s): Fluka 56690; Sigma H9252.

Derivative: *Hexabenzoyl*
Chapman & Hall Number: HJG18-W
Molecular Weight: M 1129.1.
Physical Description: Yellow leaflets.
Melting Point: Mp 304-305° (228°).

Derivative: *2,5-Dichloro*
Synonym(s): **7,7′-Dichlorohypericin**
Chapman & Hall Number: NRN67-L
Type of Compound Code(s): VQ6000, VQ9000
Molecular Formula: $C_{30}H_{14}Cl_2O_8$
Molecular Weight: M 573.341.
Source/Synthesis: Constit. of the lichens *Heterodermia obscurata* and *Nephroma laevigatum*.
Physical Description: Purple cryst. (AcOH).
Melting Point: Mp 350°.

Derivative: *2,5,9,12-Tetrachloro*
Synonym(s): **2,2′,7,7′-Tetrachlorohypericin**
Chapman & Hall Number: NRN68-M
Type of Compound Code(s): VQ6000, VQ9000
Molecular Formula: $C_{30}H_{12}Cl_4O_8$
Molecular Weight: M 642.231.
Source/Synthesis: Constit. of *Nephroma laevigatum*.
Physical Description: Purple cryst. (AcOH).
Melting Point: Mp 350°.

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