

General article Γενικό άρθρο

History and therapeutic properties of *Hypericum Perforatum* from antiquity until today

C.I. Istikoglou,¹ V. Mavreas,² G. Geroulanos¹

¹Department of Psychiatry, "Konstantopouleion" General Hospital, Nea Ionia, Athens,

²Medical School, University of Ioannina, Ioannina, Greece

Psychiatriki 2010, 21:332–338

The St. John's wort has been recently one of the most popular therapeutic means that may be easily found in health food stores in various forms, such as capsules, liquid extracts, oils, ointments and others. The St. John's wort is not, however, a new pharmaceutical aid. The herb has a long and particular background as an antidepressant, anti-septic, anti-inflammatory, expectorant and tonic for the immune system, used for its alleviating properties. In fact, some of the previous reports on the herb's use originate from the Greek herbalist of the 1st AD century, Pedanios Dioscorides, as well as from his contemporary physicians, respectively Greek and Roman, Galenos and Plinius. In the treatise, Paracelsus (1493–1541 AD), the famous Swiss alchemist and physician, has been also mentioned to be using the St. John's wort. The historians consider that the name of the St. John's wort was given to it by the first Christians, who noticed that the plant blossoms on about the 24th of June, the Saint John's-the Baptist's birthday, who was decapitated. In our times, and mainly in the USA, the UK and Germany, the St. John's wort has been extensively used for the treatment of mild and moderate depression. According to researchers, the St. John's wort has an action equivalent to amitriptyline, fluoxetine and maprotiline, and is clearly more active than placebo. Experimental protocols have been also in progress on the St. John's wort therapeutic action against diseases of our times, such as cancer, AIDS and hepatitis. According to what is widely supported, the St. John's wort is considered as bridge between the conventional and the alternative medicine. The St. John's wort pharmacodynamics as well as pharmacokinetics have been also extensively studied. The probable mechanism of the St. John's wort action is the suspension of monoaminoxidase (MAO) and the suspended reuptake of serotonin. Using the St. John's wort we open the wide sphere of natural therapies. Such an extended approach may lead us to an increasing evaluation of our natural sources. Preserving what we have and renewing what we have destroyed is our only hope for the future of humanity, our planet and all the living organisms.

Key words: St. John's wort, depression, antiquity, Dioscorides, serotonin

Introduction

Hypericum Perforatum or St. John's Wort, has been one of the most popular therapeutic means during these past years. It can be easily commercially acquired, in various forms, i.e. capsules, liquid extracts, oils, ointments, etc. Nevertheless, hypericum is not a new treatment aid. This herb has a long and special history as an anti-depressant, antiseptic, anti-inflammatory, expectorant, immune system tonic, and lenitive.¹⁻³

For centuries, the Europeans have been using it in order to treat a vast number of diseases, like anxiety, colds, depression, flue, haemorrhoids, womb muscle contractions during menstruation, skin infections, and wounds. In reality, several of the older references to the use of this herb for haematoma, burns, wounds and skin irritations, come from the Greek herbologist of the 1st century a.c., Dioscorides, the roman student of the 1st century a.c., Plinius, and the Greek doctor of the 5th century b.c., the father of Medicine, Hippocrates.⁴⁻⁶

Hypericum is being developed in North America and Australia, but this plant also breeds in Europe, where it flourishes in open fields, in dry riverbeds, on rocky planes, in city parks and gardens. Historians think that the name "St. John's Wort" has been given by the first Christians, who noticed that it flourishes around the 24th of June, at the birthday of St. John the Baptist, who has been beheaded.

Hypericum belongs in the class of teoids, the family of hypericides, and it is a herbaceous, brushwood or bushy, perennial plant, with yellow, spoke-like flowers and small, long leaves.

Hypericum's main properties are: (1) Quinones: hypericin, pseudohypericin, hyperphorin, (2) Flavonoids: hypericin, quercetin, diflavone, proanthocyanidin, amentoflavone, (3) Essential/volatile Oils, (4) Xanthones, (5) Tannines, and (6) Coumarins: umbelliferone, scopoletin.⁶

Purpose

Despite the relatively poor bibliography, regarding the action of Hypericum during antiquity, several

articles have been published regarding its history, as well as bibliographic references of Dioscorides, Galen and Paracelsus. The purpose of this work is to show the important and numerous applications the Hypericum has, for the treatment of many medical indications, from antiquity until today.

Many researches and valid medical articles are also quoted, regarding depression, which today is the main therapeutic indication of Hypericum.

An important purpose of the present thesis is to present the history of Hypericum, a travel in time, from antiquity until today.⁷

Material and method

Many bibliographic references are quoted, among which several books and articles, dealing with the history and therapeutic properties of the Hypericum from antiquity until today.

Results

Long before drugs were invented, herbs were proved to have strong therapeutic properties. Among herbs, Hypericum has a prominent position, and it is well known for its therapeutic properties, since antiquity. One could say that Saint John's Wort is the point where magic and myth meet Medicine.⁹

Hypericum Perforatum has crossed an impressive path, from its popular use during antiquity, where its use was covered both in practice and imagination, until its recent remarkable status as a miracle-herb for the modern world, where it can constitute the crucial, final bond between alternative and conventional medicine.⁵

Regarding Hypericum's history, the first to describe the therapeutic properties of the plant as a healing, diuretic, analgesic, and a drug antimalaria, was Pedanius Dioscorides, the most popular pharmacologist of antiquity, who lived in the 1st century a.c. Dioscorides served as a military physician, near Cladius and Nero. The first medical material recorded in the West, in particular a synopsis regarding plants, is owed to him. In his notorious work, "About Medical Material", he describes Hypericum as follows: "It is a

big, tufted, red bush; its flower resembles the leucoia and, if rubbed between the fingers, it produces a juice that resembles human blood. For this reason the plant has been named Androhaïmon (human blood)". His contemporary physicians, Greek and Roman respectively, Galen and Plinius, repeated important references to the plant of Dioscorides, while other physicians of the time remarked that Saint John's Wort was an excellent drug to provoke menstruation, and an antipyretic. Furthermore, Plinius the Roman, found it extremely effective for the healing of snake bites, when mixed with wine. Dioscorides writes on Hypericum: «ΥΠΕΡΙΚΟΝ. ΟΙ ΔΕ ΑΣΚΥΡΟΝ ΟΙ ΔΕ ΑΣΚΥΡΟΪΔΕΣ, ΟΙ ΔΕ ΑΝΔΡΟΣΑΙΜΟΝ. ΚΑΙ ΤΟΥΤΟ ΕΣΤΙΝ ΕΙΔΟΣ ΥΠΕΡΙΚΟΥ ΔΙΑΦΕΡΟΝ ΚΛΩΣΙΝ, ΦΡΥΓΑΝΩΔΕΣΤΕΡΟΝ ΔΕ ΚΑΙ ΠΕΦΟΙΝΙΓΜΕΝΟΝ ΤΟΙΣ ΦΥΛΛΟΙΣ ΛΕΠΤΟΙΣ, ΑΝΘΗ ΜΗΛΙΝΑ, ΚΑΡΠΟΝ ΔΕ ΟΜΟΙΟΝ ΥΠΕΡΙΚΩ, ΟΖΟΝΤΑ ΡΗΤΕΙΝΗΝ ΚΑΙ ΟΙΟΝΕΙ ΑΙΜΑΚΟΝΤΑ ΤΟΥΣ ΔΑΚΤΥΛΟΥΣ, ΤΟ ΣΠΕΡΜΑ ΩΣΤΕ ΔΙΑ ΤΟΥΤΟ ΑΝΔΡΟΣΑΙΜΟΝ ΚΑΛΕΙΤΑΙ. ΠΟΕΙ ΔΕ ΚΑΙ ΤΟΥΤΟΥ Ο ΚΑΡΠΟΣ ΠΡΟΣ ΙΣΚΙΑΔΙΚΟΥΣ ΠΕΙΝΟΜΕΝΟΣ ΜΕΘ'ΥΔΡΟΜΕΛΙΤΟΣ ΚΟΤΥΛΩ ΔΥΕΙΝ. ΑΓΕΙ ΔΕ ΧΟΛΩΔΗ ΚΑΙ ΚΟΠΡΙΑ ΠΟΛΛΑ ΣΥΝΕΧΩΣ ΔΙΔΟΜΕΝΟΣ ΑΧΡΙ ΑΝ ΥΓΙΑΣΘΩΣΙΝ ΠΟΕΙ ΚΑΙ ΠΡΟΣ ΠΥΡΙΣΑΥΤΑ ΕΠΙΠΛΑΣΘΕΙΣ:», Φ. 145, σελ. 206 ΠΕΡΙ ΥΛΗΣ ΙΑΤΡΙΚΗΣ, Ο ΕΛΛΗΝΙΚΟΣ ΚΩΔΙΚΑΣ 1, ΤΗΣ ΕΘΝΙΚΗΣ ΒΙΒΛΙΟΘΗΚΗΣ ΤΗΣ ΝΕΑΠΟΛΕΩΣ, ΕΙΣΑΓΩΓΙΚΑ ΚΕΙΜΕΝΑ.¹⁰⁻¹⁴

In fact, most of the initial recorded references come from people that used herbs and physicians that lived in Greece and the Roman Empire, where the plant was known with its Greek name "Υπερικον". Like most famous herbs, the healing properties of which have been appreciated for centuries, the benefits from Saint John's Wort have been known beyond doubt, and passed on from mouth to mouth through generations of votanologists and healers, before history itself. For instance, the effectiveness of Saint John's Wort for the healing of wounds and inflammations was surely known for some time then. Most of the early healers followed the old popular belief that the natural characteristics of any therapeutic drug were related to the conditions under which treatment is more effective. The oil extracted flowers and plants from looked like blood, made the ancient people that

think this plant would be effective in the treatment of wounds and inflammatory infections – and that was true.¹⁵⁻¹⁹

Paracelsus was the first to discover the importance of sterilizing Hypericum with boiling, while recommending it for the treatment of ill temper and anxiety. Since then, Hypericum is an ingredient of a "natural drug".

Furthermore, should it be noted that during the 6th century, as mentioned in an inscription, the plant has been immortalized by the Celt Saint Coloumba, who was devoted to Saint John the Baptist. Saint Coloumba, who founded monasteries all over Ireland and Scotland, is said that carried a branch of Hypericum or Saint John's Wort with him everywhere he went, in honour of the martyred Saint. Furthermore, according to a tradition, he brought Saint John's wort with him as spiritual protection during his long and dangerous journeys as a missionary to Celtic tribes.

Until the Middle Ages, Hypericum formed a part of many summer solstice rituals. In the eve of Saint John's day, for instance, people used to hang garlands made of the leaves and flowers of this plant over the doors of houses and churches, to protect them from witches and evil spirits. People also used to put branches of this plant under their pillows in the eve of Saint John's day, believing that the Saint himself would appear to them in a dream, give them his blessing, and keep death away for the year to come. The dried leaves of the plant were considered to be protective talismans, used like bookmarks within the Bible and prayer books.

It is easy for one to understand the way in which several of these ancient superstitions came up. This plant flourishes mildly and copiously, near the date of the summer solstice, an important time of planting, accompanied by a wealth of pagan, indigenous and early religious rituals. People performed sacrifices and offerings to ancient Gods, like the Sun and the Earth, for the fertility of the season. Prayers were made to the Gods of the West, to bring a copious harvest during the Fall.

Furthermore, this is the time when we celebrate the birthday of Saint John the Baptist, who was

tragically beheaded, and his head was offered to Salome. This last part, along with the fact that the plant's oil leave blood-like stains on the fingers and the hands of those gathering it, provoked some interest regarding certain of the magical and sinister and implicits regarding Saint John's Plant. Moreover, in antiquity, it was believed that Saint John's Wort offered protection from evil spirits and bad luck; this belief may have originated partly from the plant's initial use by traditional healers as a drug for the so-called "melancholy", or troubled minds. Today, we call these conditions "depression" or "anxiety".

Indeed, Hypericum has recently attracted considerable attention, for its anti-depressant properties. In any case, during antiquity, the effectiveness of the use of this plant for the treatment of any mental or emotional condition, has been undoubtedly proven, although not fully appreciated, as a side-effect of one of its more common uses. Ancient healers and herbologists, who usually treated wounds and infections using this plant, possibly noticed that the plant also had a tranquillizing effect, especially in its clear oil form, when applied directly and absorbed by the skin, and in its liquid form (derived by the steam created by its leaves and flowers – called a "concoction" in traditional herbology) administered orally.

Later, the Crusaders brought the plant with them to protect themselves by witchcraft; they also used soaked flowers and leaves as ointments to treat the wounds of battle. Naturally, until the Middle Ages, all these therapeutic uses were common practice. The Knights of the Order of Saint John of Jerusalem regularly used cataplasms made of mashed flowers and leaves of this plant, to contain bleeding and heal the wounds of battle, during the 11th, 12th, and 13th century. During the same period, the people suffering from rage, or believed to have been possessed by daemons, often were administered concoctions of the plant, or inhaled its slightly bitter and acid smell.^{20,21}

In 1618, Hypericum was one of the therapeutic plants to be mentioned in the first London Pharmacopeia. In England, the plant has been made

particularly known by Nicholas Culpeper (1616–1654), the famous botanologist.

The American settlers that immigrated to England, France, and Germany, brought the plant to the North Eastern states of the USA, and from there, it has spread to the argest part of the country, as the settlers moved towards the South and the West. One hundred years later, during the Eclectic Period, the golden age of American herbology, known herbologists like John King and Finley Ellingwood marked that the use of Hypericum had now spread beyond the healing of wounds, and that the drug was now used as a diuretic, astringent, tranquilliser, and for the treatment of depression. Nevertheless, during the 20th century, Hypericum became known for its vast treatment applications, mainly as an anti-depressant, in both sides of the Atlantic.

The treatment indications of the Hypericum, from antiquity until today, is common cold, the flu, infectious mononucleosis, dysmenorrhea, menopause, premenstrual dystonia, carpal tunnel syndrome, lumbago, strains, carbuncles, subcutaneous haematoma, burns of all natures, insect bites, obesity, anxiety, insomnia, seasonal emotional disturbance, and, finally, mild and moderate depression.^{21,22}

Discussion

Based on bibliography, it seems that the Hypericum has been known since antiquity for its vast treatment applications. Today, especially in the USA, United Kingdom and Germany, it is administered for the treatment of mild and moderate depression. Its Pharmacodynamics and Pharmacokinetics have been extensively studied, and many research protocols are under development for the vaster treatment of many serious conditions like cancer, HIV and hepatitis, as well as comparative studies of Hypericum with the activity of tricyclic antidepressants (TCA), and serotonin reuptake inhibitors (SSRI). According to relatively older studies, the Hypericum has equal activity with amitryptiline, fluoxetine and maprotiline, while clearly exceeds activity versus placebo. According to its possible mechanism of activity, it is consid-

ered to be a monoaminoxidase inhibitor (MAO) and an inhibitor of serotonin reuptake.²²⁻²⁹

Conclusions

In the present thesis, we have studied the function of Saint John's Wort, as well as the time and method of its application to treat depression, and the rest of its therapeutic applications. Furthermore, its history has been studied based on bibliographic resources, mainly the work of eminent roman physician and botanologist Pedanius Dioscorides, in the 5th cent. a.c. Also, we have examined its effectiveness, as well as all comparative studies with synthetic anti-depressants, and protocols under development, regarding the treatment properties of Hypericum in many other illness conditions of our times.

People suffering with mild and moderate depression can be treated successfully with Saint John's Wort, without having to sacrifice their quality of life or their health. This herb comprises an unusual combination of safety, effectiveness, a vast scale of benefits, a lack of serious side-effects and low cost. An extensive European research on Saint John's Wort has had positive results, and the National Mental Health Institution of the USA, is now conducting a proprietary research worth 4.3 billion dollars, comparing the Hypericum to a placebo and the known pharmaceutical anti-depressants.

The popularity of Hypericum (St. John's Wort), has renewed the people's recognition and acceptance

of natural drugs, through average people that look beyond conventional medicine to find solution in their problems of health. By all means, these people should not diagnose themselves, or follow a treatment of their own contrivance. In any case, there are financial aspects that make specialized help non-available to many people. In any case, treatment with Saint John's Wort without a prescription is frequently needed. We make a part of nature, and natural substances are more compatible with human biology than synthetic substances. Our dependence from technological medicine, including pharmaceutical products, did not sufficiently free people of the disease. The increase of expenses on health also urges the need to use these even less expensive products.

This is a wonderful moment for one to be a doctor, with a multitude of new treatment possibilities opening every day. We also observe that most doctors have been motivated and have the curiosity to establish the best, less harmful methods to help their patients.

Let us use Hypericum as a bridge between established and alternative treatments, and let us continue to enlarge the vast sphere of natural treatments. This extensive approach can lead us to an increasing appreciation of our natural resources. Preserving what we have destroyed is our only hope for the future of mankind, the planet, and all living organisms.^{30,31}

Ιστορία και θεραπευτικές ιδιότητες του *Hypericum Perforatum* από την αρχαιότητα έως σήμερα

Χ.Ι. Ιστίκογλου,¹ Β. Μαυρέας,² Σ. Γερουλάνος¹

¹Τμήμα Ψυχιατρικής, ΓΝ «Κωνσταντοπούλειο», Νέα Ιωνία, Αττική,

²Ιατρική Σχολή, Πανεπιστήμιο Ιωαννίνων, Ιωάννινα

Ψυχιατρική 2010, 21:332–338

Πρόσφατα διαπιστώθηκε ότι το Υπέρικο είναι ένα από τα δημοφιλέστερα θεραπευτικά μέσα που βρίσκει κανείς εύκολα σε καταστήματα προϊόντων υγιεινής διατροφής με διάφορες μορφές, όπως κάψουλες, υγρά εκχυλίσματα, έλαια, αλοιφές και άλλα. Το Υπέρικο δεν είναι ωστόσο νέο φαρμακευτικό προϊόν. Το βότανο αυτό έχει μακρά και ιδιαίτερη ιστορία ως αντικαταθλιπτικό, αντισηπτικό, αντιφλεγμονώδες και αποχρεμπτικό φάρμακο και ως τονωτικό του ανοσοποιητικού συστήματος, ενώ χρησιμοποιήθηκε επίσης και για τις καταπραυντικές του ιδιότητες. Ορισμένες από τις παραπάνω αναφορές στις χρήσεις του προϊόντος καταγράφηκαν από τον Έλληνα βοτανολόγο του 1ου μ.Χ. αιώνα Πεδάνιο Διοσκουρίδη και στους σύγχρονους του ιατρούς, τον Έλληνα Γαληνό και το Ρωμαίο Πλήνιο. Στην πραγματεία αναφέρεται επίσης ότι και ο διάσημος Ελβετός αλχημιστής και ιατρός Παράκελσος (1493–1541 μ.Χ.) γνώριζε και χρησιμοποιούσε το Υπερικό. Σύμφωνα με τους ιστορικούς, το Υπέρικο πήρε το όνομα του (St. John's wort – βότανο του Αγ. Ιωάννη) από τους πρώτους χριστιανούς που παρατήρησαν ότι ανθίζει γύρω στις 24 Ιουνίου, γενέθλιο του Αγ. Ιωάννη του Βαπτιστή. Στις μέρες μας και κυρίως στις ΗΠΑ, το Ηνωμένο Βασίλειο και τη Γερμανία, το Υπέρικο χρησιμοποιείται εκτεταμένα για τη θεραπεία της ήπιας και μέτριας κατάθλιψης. Σύμφωνα με τους ερευνητές, το Υπέρικο δρα παρόμοια με την αμιτρυπτιλίνη, τη φλουοξετίνη και τη μαπροτιλίνη και είναι οπωσδήποτε πιο ενεργό από το έκδοχο. Πειραματικά πρωτόκολλα σχετικά με τη θεραπευτική δράση του Υπερικού κατά σύγχρονων νοσημάτων όπως ο καρκίνος, το AIDS και η ηπατίτιδα βρίσκονται αυτή τη στιγμή σε εξέλιξη. Κατά κοινή ομολογία, το Υπερικό γεφυρώνει τη συμβατική με την εναλλακτική ιατρική. Η φαρμακοδυναμική, όπως και η φαρμακοκινητική του Υπερικού έχει επίσης μελετηθεί εκτεταμένα. Ο ενδεχόμενος μηχανισμός δράσης του Υπερικού είναι η αναστολή της μονοαμινοξειδάσης (MAO) και η αναστολή επαναπρόσληψης της σεροτονίνης. Με τη χρήση του Υπερικού, ανοίγει ένα παράθυρο στο μεγάλο κόσμο των φυσικών θεραπειών. Μια τόσο εκτεταμένη προσέγγιση ενδέχεται να μας οδηγήσει σε αυξανόμενη επαναξιολόγηση των φυσικών μας πόρων. Το να διατηρούμε όσα έχουμε και να ανανεώσουμε όσα καταστρέψαμε είναι η μόνη ελπίδα για το μέλλον της ανθρωπότητας, του πλανήτη μας και των ζωντανών οργανισμών.

Λέξεις ευρετηρίου: υπέρικον, κατάθλιψη, αρχαιότητα, Διοσκουρίδης, σεροτονίνη

References

1. Λεξικόν Δημητράκου, σελ. 7413
2. Λεξικό Ελευθερουδάκη, σελ. 464
3. Βοτανολογία Γενναδίου, σελ. 986
4. Pedersen S. *St. John's Wort*. Dorling Kindersley, New York 2001:6–11
5. Poldinger W. Zur Geschichte des Johannis Kraut. *Schweitz Rundsch Med Prax* 2000, 89:2102–2109
6. Pressman A. *St. John's Wort: the miracle medicine*. The Philip Lief Group Inc., New York, 1998:3–11
7. Le Strange R. *A history of herbal plants*. Arco Publishing, New York, 1977
8. American Herbal Pharmacopoeia™ and Therapeutic Compendium. Monograph: St. John's Wort. American Herbal Pharmacopoeia™, Santa Cruz-CA, 1997
9. Scarborough J. *Pharmacy's ancient heritage: Theophrastus, Nicander and Dioscurides*. The Distinguished Lectures 1984, College of Pharmacy, University of Kentucky, Lexington 1985
10. Διοσκουρίδης. *Περί ύλης ιατρικής*. (Α΄ Τόμος). Εκδόσεις Κάκτος, Αθήνα, 2000:11–27
11. Διοσκουρίδης. *Περί ύλης ιατρικής*. Ο Ελληνικός κώδικας 1, της εθνικής βιβλιοθήκης της Νεαπόλεως, εισαγωγικά κείμενα, Φ. 145, σελ. 206
12. Max Wellman. Dioscurides 12. In: *Realencyclopädie der Klassischen Altertumswissenschaft*. Vol. V, 1. Stuttgart 1903: 1131–1142
13. Riddle JM. *Dioscurides on pharmacy and medicine*. History of Science Series, No 3, Austin, 1985
14. Pedanii Dioscurides Anazarbei. *De material medica libri quinque*. Edidit Max Wellman. 3 vols. Berlin 1906–1914 (reprint: Berlin 1958)
15. Berendes J. *Des Pedanios Dioscurides aus Anazarbos Arzneimittellehre in fünf Büchern. Übersetzt und mit erläuterungen versehen von*. Stuttgart 1902 (several reprints; recently: Graz, 1988)
16. The Greek herbal of Dioscurides illustrated by a Byzantine A.D. 512, Englished by John Goodyer A.D. 1655. Edited and first printed A.D. 1933 by Robert T. Gunther, New York 1934 (several reprints, the most recent of which is: New York 1968)
17. Dioscurides, Plantas y remedios medicinales (De material medica). Introduction, traducción y notas de Manuela Garcva Valdés, 2 vols. (Biblioteca clásica Gredos, 253–254), Madrid 1998
18. Alain Touwaide. Le strategie terapeutiche: i farmaci, in Storia del pensiero medico occidentale. A cura di Mirko D. Grmek. Volume 1: Antichità e Medioevo, Bari & Roma 1993:349–369
19. Alain Touwaide. La therapeutique medicamenteuse de Dioskoride à Galien: du pharmaco-centrisme au medico-centrisme. In: Armelle Debru (ed) *Galien on pharmacology. Philosophy, history and medicine*. (Studies in ancient medicine, 16), Leiden, New York, Koln, 1997:255–282
20. Pressman A. *St. John's Wort: the miracle medicine. Getting to know the plant's constituents*. The Philip Lief Group Inc., New York, 1998:20–21
21. Hahn G. Hypericum Perforatum (St. John's wort) – a medicinal herb used in antiquity and still of interest today. *J Naturopath Med* 1992, 3:94–96
22. Linde K et al. St. John's wort for depression: an overview and meta-analysis of randomized clinical trials. *Br Med J* 1996, 313:253–258
23. Bladt S, Wagner H. Inhibition of MAO by fractions and constituents of Hypericum extract. *J Geriatr Psychiatry Neurol* 1994, 7(Suppl 1):S57–S59
24. Bloomfield HH, McWilliams P. *Hypericum for depression*. Prelude Press, Los Angeles, 1996
25. Ernst E. St. John's wort, an antidepressant? A systematic, criteria based review. *Phytomedicine* 1995, 2:47–71
26. Harrer G. Clinical Investigation of the antidepressant effectiveness of Hypericum. *J Geriatr Psychiatry Neurol* 1994, 7:S6–S8
27. Biglia AR, Hagsen S. *HYPERIC HERBA: St. John's wort ESCOP*. Proposal for the summary of product characteristics. Interaction with other medicaments and other forms of interaction, 2002:6
28. Müller WE, Rossol R. Effects of Hypericum extract on the suppression of serotonin receptors. *J Geriatr Psychiatry Neurol* 1994, 7(Suppl 1):S63–S64
29. Beckman SE, Sommi RW, Switzer J. Consumer use of St. John's wort: a survey on effectiveness, safety and tolerability. *Pharmacotherapy* 2000, 20:568–574
30. Saltzman C. St. John's wort. *Harv Rev Psychiatry* 1998, 5:323–325
31. Greeson JM, Sanford B, Mont DA. St. John's wort (Hypericum Perforatum): a review of the current pharmacological, toxicological and clinical literature. *Psychopharmacology* 2001, 153:402–414

Corresponding author: C.I. Istikoglou, Psychiatrist, "Konstantopouleion" General Hospital, Nea Ionia, Athens
Tel.: +30210-27 92 844, 6944 595 933, Fax: +30210-27 96 273