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DEPRESSION
PART I: From PROZAC to ST. JOHN'S WORT

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Symptoms of depression, such as unhappiness and disappointment, are common, affecting up to a third of the population. When symptoms become pervasive, severely affect the quality of life, or interfere with normal function, they are considered pathological. The clinical syndrome is called depressive disorder, major depression, or clinical depression. Other diagnoses include melancholia (a subtype of depression), bipolar affective disorder (episodes of major depression and episodes of mania), dysthmia (intermittent depressive symptoms), recurrent brief depression (less severe than major depression), and minor depression (by degree less severe and of shorter duration than major depression). The list continually grows to categorize and label various aspects of this epidemic.

Studies show that more than 17 million Americans suffer from depression and the number keeps rising. Major depression affects 25% of adult women in America and 12% of men. WHO estimates that major depression will be one of the most important overall causes of ill health in this new century. The cause of depression "is still obscure," but that "a number of diverse factors are likely to be implicated." Treatment must involve a variety of methods.

There are 10 "official" symptoms that may characterize a major depressive episode, though if five are present, this diagnosis is usually made. They include:

- Persistent feelings of sadness, emptiness, pessimism, or hopelessness.
- Feelings of worthlessness, helplessness, guilt.
- Loss of interest or pleasure in activities, including sex.
- Decreased or increased sleep.
- Decreased or increased appetite with weight loss or gain.
- Decreased energy; fatigue, lethargy.
- Difficulty concentrating, remembering, or making decisions.
- Restlessness, irritability.
- Thoughts of death or suicide.
- Various pains, such as headaches or chest pain, that are not accompanied by any evidence of disease.

Sadly, there is a linear, mechanistic viewpoint towards this affliction. "Depression is a major health concern not only because of personal distress, excess mortality, impaired interpersonal relationships, and restriction of work activities but also because of the economic burden it imposes." The estimated cost in the U.S. for 1990 was $53 million, comparable with cancer, coronary heart disease, and AIDS. Doctors are urged to be "more aggressive" in diagnosing and treating depression and to prescribe "antidepressant medicines."

A person suffering with depression only knows there is sadness, despondency, hopelessness, a continuing feeling that life is not worth living. Relief is desperately sought. Attempts are made to get as far away as possible from the bleakness – as quickly as possible. So a prescription for an antidepressant drug seems ideal. But is a drug only a chemical refuge? Does it truly "cure" the problem? What of the unnecessary side effects and health risks? Do drugs permit the sufferer to bypass or disregard the cause(s) of the depression, allowing the underlying problems to putrefy and fester?

There is no question that the "treatment" of depression is "undergoing a trend toward drugs and away from talk therapy." There are many physiological, biochemical, psychological, and even spiritual aspects to depression. Yet drugs are seen as more efficient, more cost effective, easier to deal with. The prescription pack is led by Prozac, the new generation wonder drug. [i]

PROZAC ET AL

The two drug families which were traditionally used as antidepressants are **triclyclics** and **MAOIs** (monoamine-oxidate inhibitors). Tricylcics, in particular, had been the mainstay of treatment for years. These and MAOIs "apparently" boost levels of neurotransmitters (chemical messengers) "thought to be low" in the brains of depressed people. Tricyclics include amitriptyline (Elavil, Endep), desipramine (Norpramin, Pertofrane), imipramine (Janimine, Tofranil), nortriptyline (Aventryl, Pamelor).

MAOIs include isocarboxazid (Marplan), phenelzine (Nardil), and tranylcypromine (Parnate). A patient must take the drug for at least three weeks before mood improves. Both types of drugs require close monitoring to determine proper dosage. And the side effects can be severe and debilitating. Tricyclics, for example, can induce dry mouth (and resultant dental problems), constipation, weight gain, blurred vision, heart attacks, stroke, high or low blood pressure, heart block, seizures, hallucinations, delusions, confusion, disorientation, incoordination, peripheral neuropathy, tremors, numbness, tingling, abnormal involuntary movements, anxiety, insomnia, nightmares, dizziness, weakness, fatigue, urinary retention, increased ocular pressure, rashes, bone marrow depression, elevation or lowering of blood sugar, edema, hair loss, etc. MAOIs can provoke the same side effects plus an increased risk of hypertension and chronic hepatitis; patients must avoid wine, beer, pickles, cheese, liver, sauerkraut, yogurt, yeast, and other aged or fermented foods.

Prozac (fluoxetine) made its debut in 1987 to usher in a new generation of antidepressant drugs, Selective Serotonin Reuptake Inhibitors (SSRIs). Along with Prozac, there are now several other SSRIs and related drugs and the value in the world market is over four billion dollars a year. Underlying the success of the SSRIs has been the widely promoted theory that depression is a serotonin-deficiency disease -- that depression is simply a biological affliction just as diabetes is viewed as a lack of insulin. The notion that depression is generally caused by lack of serotonin (or some simple imbalance of other neurotransmitters) does not explain many questions and experiences. A few problems with this line of thinking are: Why do drugs which have an immediate effect in raising brain serotonin levels usually take at least a couple of weeks to exert an antidepressant effect? Why do SSRIs have no more effect on depression than other antidepressants which hardly act on serotonin? Why do antidepressants lack an effect on the most clear-cut cases of depression, about one-quarter of all cases most resistant to treatment with drugs? How to SSRIs reduce despondence of the depressed, alleviate anxiety in the fearful, and change the outlook of those who are sensitive to rejection, as well as create other personality changes that occur? "Are the personality changes…really due to Prozac's pharmacological effects, or is the drug just an expensive placebo?"

Prozac's popularity in part derives – not from its efficacy (which is no greater than other types of antidepressants), but rather from its promotion as having less objectionable side effects. Another reason for its popularity has been the best seller book, *Listening to Prozac*, by psychiatrist Peter Kramer whose enthusiasm for the use of this drug to transform people's behavior led to its widespread prescription.

An analysis of 63 trials, however, showed that only three percent fewer participants quit an SSRI because of side effects, with no difference in overall dropout rates or for dropouts due to lack of efficacy. Little advantage to SSRIs is indicated by the flow of spontaneous reports of suspected adverse reactions. Keeping in mind that relatively few suspected adverse reactions are actually reported (even serious and fatal reactions are usually reported at less than one in 10), reports for the three main SSRIs -- after fewer than 10 years in use -- approximate the total numbers reported for all prescribed drugs in one year and far exceed the numbers for supposedly more troublesome antidepressants. Of course, SSRIs are prescribed in large numbers. But there is little to indicate any distinct advantages to Prozac or other SSRIs.

Commonly (affecting 5% to 25% of patients) recognized SSRI side effects include agitation, anxiety, headache, dizziness, insomnia, nausea, nervousness, drowsiness, sweating, diarrhea, somnolence, and tremor. Risk of gastro-intestinal bleeding is greatly increased, particularly when taken with non-steroidal anti-inflammatory drugs or aspirin. Less reported are loss of libido, sexual dysfunction, painful menstruation, urinary tract inflammation, hives and other rashes, hair loss, arthritis, hot flushes, palpitations, aplastic anemia, confusion, impaired concentration, abnormal dreaming, nightmares, amnesia, liver disorders. Disconcerting are the reports relating to aggression, hallucinations, fatigue, malaise, and depersonalization. When taken during the first trimester of pregnancy, Prozac increases the chance that a baby would be born with three or more minor malformations, such as fused toes. Continuation during the third trimester of pregnancy increases the risk of premature delivery and delivering small babies suffering from a variety of health problems. SSRIs can cause a broad spectrum of neurological and psychological side effects, over-stimulating some and sedating others. "A small [?] percentage of patients become violent or more suicidal." Doctors need to keep "closer tabs on these patients." Yet, "Prozac's ease of use has made some doctors lax." There is no denying that "the effects of antidepressants can vary

considerably." Furthermore, there is "increasing evidence that a combination of medication and psychotherapy may be the best approach for depression." Do the benefits of drugs like Prozac truly outweigh the detriments? Actually, an analysis of controlled studies found that more than half of those taking Prozac experienced adverse effects, and 20% of subjects stopped taking the drug because of these problems. And Prozac does not "work" for everyone – it is "pretty hit-or-miss."

It is admitted that – even today – advances in clinical psychopharmacology "have not come about by elegant deduction from an understanding of how the brain controls behavior but instead by chance discoveries based on fragments of information." This confidence-shaking fact shows that scientists do not have to understand the brain or the roots of human behavior in order to make drugs that can specifically interfere with its neurotransmitters and the receptors they act on. There is much they still do not know. For instance, a new study suggests that SSRIs may boost the efficiency of brain enzymes that make several steroid hormones. What effects could excess steroid production elicit? Not yet known. The orthodox medical opinion may reassuringly state that drugs benefit only people with clinical conditions and should only be used by them. But in reality, almost anything that responds to drugs can become a medical "condition."

Peter Kramer and others argue that Prozac enhances feelings of social ease and flexibility in people who constantly fear rejection by others but do not suffer from full-blown depression. "Personality disorders" attract the use of Prozac and its chemical cousins. The five million Americans "said" to be suffering from obsessive-compulsive disorder are targeted as consumers for Prozac. It "may" be helpful in treating both obesity and bulimia nervosa. The drug is viewed by some as a "possible" enhancer of sports performance. Women with depression secondary to PMS are being prescribed Prozac. Children who are fidgety in school progress from Ritalin to Prozac. Migraine sufferers are encouraged to try it. Many doctors have "effectively expanded the definition of what constitutes clinical depression to include chronic low-grade depression (dysthymia) and have, in some cases, prescribed Prozac to "otherwise healthy patients suffering from low self-esteem or nagqing anxieties." Prozac, like other antidepressants, is capable of flipping people into mania (an "up" or hyper stage of manic depression) and can produce anxiety. In fact, the side effects are strikingly similar to those produced by **stimulant** drugs such as caffeine, cocaine, and amphetamines. Some doctors "may be" overprescribing Prozac and using it to treat "relatively trivial personality disorders," making a shy person more outgoing, for example, or a passive one more aggressive. Prozac is not being used only as a "happy pill," but is prescribed for a multitude of symptoms for which it has not been approved for use. Furthermore, Prozac has been implicated in numerous suicides and acts of violence. This and its many other reported side effects are just "the tip of the iceberg." For example, there is evidence that Prozac and some other widely used drugs "may promote the growth of cancerous tumors."

SSRIs may, according to *the International Journal of Risk and Safety in Medicine,* Volume 10, be trapping people in a "web" of dependence. There is a high incidence of withdrawal problems during discontinuation (often mistaken for a recurrence of depression) and accumulating evidence of dependency.

Prozac was not studied in people with extreme depression – such individuals were deliberately excluded from the clinical trials. Of 4,000 trial participants, only 286 Prozac-treated people actually completed the four- to six-week studies. The data show stimulant-type side effects, including agitation, irritability, excitement, nightmares, sweating, dry mouth, abnormal sensations, abnormal bodily movements, and palpitations. A condition of constant agitation, *akathisia*, may be produced in 10 to 25% of Prozac users, often in conjunction with suicidal thoughts, hostility, and violent behavior. Akathisia is both mental and physical agitation that can spark self-destructive, violent behavior, and induce dissociative reactions, making individuals who take the drug insensitive to the consequences of their behavior. According to Peter Breggin, M.D., "there is substantial evidence that many classes of psychiatric drugs – including antidepressants, such as SSRIs – can cause or exacerbate depression, suicide, paranoia and violence." The premarket testing indicated Prozac's stimulant properties "might contribute to worsening of depression.' Also, the rates of sexual dysfunction have apparently been underestimated – for Prozac and Prozac copies, Zoloft and Paxil. It is estimated that 30 to 40% of Prozac users experience reduced libido and/or problems obtaining an erection or having an orgasm, though it may help with premature ejaculation in some men. The "good" effects of the drug are questionable – it seems to create a sense of detachment, diminishing or even walling off the capacity for interpersonal relations. Prozac seems to "deprive people of the essence of their personality, turning them

into zombies." This "numbness' may be interpreted as improvement in depressed people, but it can hardly be considered healthy.

Prozac and other antidepressant drugs do elicit chemical changes in the brain, but "the lion's share of their effectiveness stems from the placebo effect," according to a statistical analysis of 39 studies. Antidepressant researchers typically pretest volunteers to eliminate those who respond strongly to a placebo. And an unknown number of studies in which antidepressants fail to outperform placebos are either not submitted or not accepted for publication.

New reports indicate that older antidepressants, such as tricyclics, and newer compounds, such as SSRIs, are not only about equally effective to treat depression, but also that they ease depression about as well as or slightly better than placebo pills. Evidently antidepressants offer no advantage over drugs such as tranquilizers and anti-anxiety drugs. This adds evidence to the suspicion that SSRIs are not as specific in their actions as their manufacturers claim. Prozac, Zoloft, Luvox, Paxil, Serzone and other SSRIs are supposed to increase the amount of serotonin in the brain. But as Simon Wessely, professor of psychiatry at King's College, London, says: "There's a tremendous uncertainty about how they work. The public thinks the doctors know, but they don't. Any decent psychopharmacologist will tell you this." The psycho-dynamics can play a role in a drug's effectiveness and in results of drug trials – side effects can alert a patient they are getting an active drug rather than a placebo. "If patients know they're getting treatment, their expectation will be raised and with it their optimism that they will get better. It's a self-fulfilling prophecy."

A review of more than 300 randomised trials that evaluated medications for depression and considered evidence for some herbal remedies showed that **St. John's wort** is significantly more effective than placebo – often as effective as drugs -- for short-term treatment of mild to moderately severe depressive disorders. What does the evidence indicate about this herb? [ii]

ST JOHN'S WORT

St. John's wort (SJW) is named after John the Baptist due to the legend during the Middle Ages that the red pigment from the flowers sprang from the blood of John the Baptist. "Wort" is an old English name for an herb thought to be related to the modern "worth" – worts were plants of worth. The history of SJW dates back to Dioscorides and Hippocrates and was used in the treatment of many illnesses. The Latin name, *hypericum perforatum*, is derived from the Greek meaning, "over an apparition." This reflects the belief that the herb conferred protection from evil spirits. Illness, particularly emotional illness and psychic pain, was believed to be caused by evil spirits and witches' spells. So SJW was apparently used to treat depression, anxiety, and other psychological ills. Now depression is viewed as strictly a biological bane. Nevertheless, although some experts claim SJW was not originally used to treat depression, its history certainly indicates it was.

This herb is described and recommended as a helpful remedy in all of the herbals down through the Middle Ages. It supports the inflammation process, is astringent, promotes wound healing, reduces pain and is sedative. It is used to treat neuralgia, anxiety, tension, and similar complaints. It is especially regarded as valuable where there are menopausal changes triggering irritability and anxiety. It also seems to ease fibrositis, sciatica, and rheumatic pain. SJW is valued as a diuretic and in treating a variety of conditions including kidney ailments, hemorrhoids, insomnia, gastritis. Externally, it can speed the healing of wounds and bruises, varicose veins, and mild burns. The oil is useful for sunburn. As occurred with many plant therapies, SJW fell from use in the late 19th century when pharmaceuticals took the forefront. Recently the herb's use was renewed, particularly in Europe, as an effective nerve tonic, helpful in cases of depression, anxiety, and unrest.

Traditionally, the leaves and flowering tops are used for their subtle therapeutic effects. Today, research usually concentrates on the "wide range of pharmacologically active compounds" including hypericin and pseudo-hypericin, flavonoids, hyperforin, xanthones, oliogomeric procyanidins, coumarins, caffeic acid, chlorogenic acid and condensed tannins. Individual chemical compounds are scrutinized for their drug-like actions rather than consideration of the whole, synergistic package. One of the components, **hypericin**, was the substance "believed" to be the main factor in the antidepressant effects. Thus the herb is usually standardized to the chemical hypericin. Recent tests indicate hypericin is not the magic ingredient. Some products are now standardized to **hyperforin**, another constituent with antidepressive action. While hyperforin "could be important" for antidepressant activity, "other compounds in the plant also contribute." Nevertheless, the tendency is to standardize products to one "active" chemical substance. Effectiveness is often judged on the basis of

studies of standardized extracts and their effects on animal cells or other chemicals in test tubes or petri dishes (*in vitro*). For example, one study concluded that such an extract "appears to exhibit a similar mode of activity in cell cultures to conventional antidepressant drugs." The human component is missing and the inert, inorganic, mechanized, linear scientific method is utilized. Problems arise in standardization. For instance, hypericin content in wild plants vary from area to area. Labels on SJW supplements will state the standardized hypericin content, but tests indicate that the products can contain as little as 47% of the hypericin listed to as much as 165% above. Why the push to standarize?

Drugs are standardized. "The" active ingredient is "known," and each dose contains the same amount of that particular ingredient. Herbs are now standardized. But if the active ingredient has not been "identified" – usually the case for herbs – and when a botanical is standardized for one or another identifiable ingredient which may not actually be the "active ingredient," and since the herb contains many other active substances, then there are mixed results and difficulties. "Pharmacists…want herbal medicines to be standardized." Herbs "should be" made into drugs. Drugs are simple. They stimulate or suppress. Pharmaceutical companies can obtain exclusive international patents and the process of manufacturing them. They can be sold for a hefty profit. Herbs like SJW confound this process. Many compounds contribute to its activity. "The variety of bioactive compounds and their effects makes the quality of some products standardized to total hypericin of dubious value, especially at this time when pure hypericin is available for 'reinforcing' the natural content of otherwise low-content products."

"Standardization" does not necessarily mean all products are consistent. There are no universally accepted methods or legal definition of standardization. Ten different manufacturers can and do "standardize" the same herb by totally different criteria and processes. The basic methods include; (1) Dissolving certain "active components" in a solvent (such as alcohol) for extraction. Chemical solvents such as benzene, hexane, acetone, methyl chloride – all toxic – are typical. Residues are commonly found in the finished product. (2) The "active component" or a synthesized (manufactured) version is added to the herb or other substances. The end product may not necessarily contain any of the whole herb. This is the cheapest and easiest method. (3) Blending various batches of herbs to obtain a hopefully more consistent product.

The first two methods are **active constituent extracts** which isolate a compound generally accepted to be "the" active one and concentrate it to a level not naturally found in the plant. This is like extracting caffeine from coffee or morphine from the opium poppy. This type of herbal extract is essentially a drug or "phytopharmaceutical." It may cause side effects not normally present in the herb or nonstandardized extract. When the isolated substance is manipulated at the expense of the whole herb's hundreds of constituents, many healing properties are lost, along with buffering compounds that reduce the possibility of adverse reactions. The third method is a **marker extract**, the "active" ingredient is unknown, so a compound characteristic to the plant is used as a "marker." Many plant constituents are present. This method does not necessarily take into account other factors such as age, growing conditions, soil nutrients, other parts of the herb, etc. New standardization methods are always being developed.

Whole herbs have been used for millennia to prevent and treat various ills and complaints. Standardized forms cannot be considered as a substitute for or an improvement on these natural plants. And yet, as SJW illustrates, the standardized herb has become so popular for treating depression that it is now difficult to find the whole, intact, non-altered form. People thus miss out on the herb's other benefits which have been known by traditional herbalists for eons. The whole SJW can be used in teas, poultices, tinctures, and powders to assist kidney problems, bronchitis, vitiligo, painful menstruation, gastritis, peptic ulcers, neuralgia, recurrent ear inflammations, gout, open wounds, and more. Just as a capsule containing ascorbic acid – so-called vitamin C – does not work the same way as foods and food complexes containing the whole vitamin C complex (with its functional components such as flavonoids, rutin, tyrosinase, K and J factors, along with associated minerals, enzymes, and other nutrients), a standardized herb does not work like the whole botanical.

Standardized herbs can be used as drugs for short periods of time in acute situations and for very specific results. But whole herbs can be used on a regular basis as needed to protect and preserve good health, to support and balance biochemistry, to supplement the diet with nutrients and other therapeutic complexes. There is a difference in **intent** of use that marks the fundamental difference between whole herb therapy and druglike phytotherapy. Whole herbs are used to support physiological and biochemical processes, the individual's condition

and constitution, so the **body** can heal itself. Druglike herbs are used to treat specific **diseases**, to stimulate or suppress physiological or biochemical processes. Many different pharmaceutical drugs have been developed to interfere in various ways with the assumed "biochemical imbalance" of depression. There is an attempt to include herbs in this class of drugs. Yet many herbalists rely on whole – not standardized – herbal products. They wish to use what has worked for many years. They like to monitor their clients carefully for the necessary doses since they know that each person's body is a little different. They realize that no food, vitamin complex, mineral complex, or herb works in the same way for everyone. As good as SJW is, it is not for everyone. With standardized herbs, the amount used is usually the amount found to be "effective" in scientific studies – without the expertise and wisdom of the herbalist and thus without individualized considerations. When knowledgeable people pick herbs, they are picked and handled in such a manner as to ensure potency. With the public demand for and commercialization of herbal products, many herbs are simply harvested to meet needs.

Standardized herbs may act more quickly (just as a drug). The majority of people have been taught to be impatient for "quick relief" and lack the understanding of natural therapies and their effects on the human system. With some helpful insight, individuals can learn to be more patient and reap a more positive outcome, knowing that all co-factors – all the biologically-active, balanced, inter-related, naturally-coordinated ingredients – are found in the whole herb as Nature wisely provided.

SJW was used for many years before depression was even considered an illness. It was used in treating nervous unrest, sleep disorders, worry, and other often vague symptoms which are now classified under the syndrome of depression. Its action supports the nerve cells, the meninges, and nerve sheaths. It was and is used for many other ailments in its intact, whole form. Its most popular use today is to allay depression -- for those who report depressed mood, occasional irritability, cognitive difficulty, social isolation, hormonal mood changes -- and it is found effective.

Physicians report that SJW benefits about 50 to 60% of users, most experiencing relief in three to four weeks. A review of 23 randomized, double-blind studies in which a total of 1,757 people with mild to moderate depression were treated with either SJW, antidepressant drugs, or a placebo, showed that the plant "performed surprisingly well." After an average of six weeks, 64% of the people taking SJW felt markedly better, compared to 59% of those receiving antidepressant drugs. "Only" 4% of the patients on SJW dropped out because of side effects (mainly mild stomach upset) while 8% of people taking standard drugs abandoned treatment. SJW has shown itself to be "remarkably safe and effective for mild to moderate depression, and even effective for major depression." The herb was 1.5 times more likely to result in an antidepressant response than placebo and was equivalent to tricyclic antidepressants. The standardized version was used in a drug-to-drug comparison.

A comparison of Prozac with SJW showed that the herb is at least as effective as Prozac in treating mild to moderate depression – according to some measures, it was more effective than Prozac. The incidence of adverse events was 23% with Prozac and 8% with standardized SJW. Again, the mentality is comparing a "natural" drug to a synthetic drug – though the herbal drug is far safer. Either way, power is taken away from the patient, physiologically and psychologically, for making changes to correct the underlying problem.

SJW may now be considered for short-term treatment of mild-acute depression according to new guidelines on the pharmacological treatment of depression from the American College of Physicians-American Society of Internal Medicine. But the herb is not yet "approved" by the FDA. Nonetheless, the standardized herb is now recognized as a drug.

With a medication mindset, some scientists think SJW is a significant monamine oxidase (MAO) inhibitor accompanied by the adverse effects of such drugs. For example, dietary restrictions would be needed to avoid the hypertensive effects. This is only 'a myth'. People taking SJW do not have to alter their diet or supplements to avoid hypertension. Many of the trials on SJW were performed in France where the diet is high in cheeses and red wine. If SJW were a MAO inhibitor, these trials would have had a very high incidence of cardiovascular events. Instead, the mechanisms of action of SJW may include serotonin and catecholamine neurotransmitters, modulation of cytokine activity, hormonal effects, photodynamic effects. However, none of these have been proven. "It is quite possible that the herb functions by a variety of these, or similar, [or other] mechanisms…"

Beyond alleviating depression, SJW has been "proven effective" in the treatment of seasonal

affective disorder, premenstrual syndrome, chronic pain disorders, postpartum depression and dysthymia. Studies show SJW improves sleep quality, often a complaint of seriously depressed people; – people sleep better and exhibit less exhaustion, sadness, helplessness, hopelessness, and headache. No side effects are reported. Externally, its oil is very soothing when rubbed on the perineum (the tear-prone area between vagina and anus) during labor of childbirth and after delivery it eases burning and swelling and accelerates healing of perineal tears. The reddish oil that oozes out when the SJW plant is handled has been shown to be useful for treating bruises, burns, cuts, and other wounds as well as insect bites, stings and scabies. In its "purified state" (isolated hyperforin), it has "antimicrobial properties" – inhibiting the growth of various bacteria including *Staphylococcus aureus* and *Candida albicans* in petri dishes. There is evidence for an "anti-inflammatory effect" of hypericin -- in the laboratory it inhibits the activity of receptor protein tyrosine kinases, insulin receptors, serine/threonine kinases, and synthesis of prostaglandin-E_2 and interleukin 6 in "treated" monocytes. As a "potent antiviral compound," hypericin "may prevent the HIV virus from entering a cell." It reduces viral "infection" in blood to be used for transfusion. "Only at high concentrations" – as a chemical drug – are some of these effects seen. Further, the actual effects on real humans may not match the laboratory recipes. Some insightful researchers recognize that there are "many other natural products derived from" SJW, so "other compounds may contribute" to its support of the inflammatory process and that "different compounds may act synergistically."

One recent study – using the LI-160 extract (a chemical isolate) of SJW or a placebo reported that, after eight weeks, SJW was no better than the sugar pill. It should be noted that this study was funded by Pfizer, the pharmaceutical company that makes Zoloft, a SSRI drug.

A trial with patients who said they felt fatigued but not depressed reported significant improvement after taking standardized SJW. Scale tests suggested that half actually were depressed and over two-thirds suffered from anxiety. After taking the herbal extract, both conditions decreased. Another study hints that the isolated substance might curb alcohol cravings in alcoholics. It "appears" to influence not only serotonin levels, but also two other neurotransmitters, dopamine and gamma-aminobutyric acid (GABA), both "thought" to play roles in alcohol addiction.

Mega-doses of SJW or, in particular, use of standardized SJW may cause numerous mild side effects. One side effect that is a photosensitizing potential of the isolated hypericin. Photosensitivity (increased sensitivity to light) is not usually observed in people taking hypericin, though it could be if taken in huge amounts for extended periods and/or it may potentiate the photosensitivity associated with tetracyclines, retin-A and other drugs known to have this effect. Grazing animals, especially cows and sheep, have had phototoxic reactions to a flower preparation – a "medication" -- of just one of 378 known species.

In humans taking standardized hypericin products, side effects are infrequent and typically mild. The most common side effects of the herbal extract include dry mouth, dizziness, nausea, gastrointestinal complaints (most commonly constipation), allergic reactions (rash), restlessness, and confusion. Laboratory monitoring shows no changes in cell counts, liver function tests, or creatinine.

A widely publicized "risk" is the "potentially" significant interaction between SJW and other drugs, including indinavir, a protease inhibitor used for HIV infection, cyclosporin, an antirejection drug used for organ transplants, digoxin used for heart stimulation, anticoagulants phenprocoumon and warfarin, the asthma drug theophylline (Theodur), and birth control pills (reduced effectiveness). Reports of substantial changes in heart rate or blood pressure "in some patients who were taking herbal medications" including SJW have been made anecdotally. Interactions with SSRI antidepressants can cause gastrointestinal discomfort, tremors, headache, restlessness, and changes in mental status.

First of all, the "herb" being tested and used is the standardized version. Second, many reports were "anecdotal' – a method severely attacked when the situation is reversed, as when benefits of whole herbs or whole food supplements are reported. In some cases, other drugs being taken by the patients could have been involved. Third, the "possible mechanisms" of some suspected effects involved induction of enzymes of the microsomal cytochrome P450 complex (which naturally and normally metabolizes or breaks down drugs) and possible interference with intestinal uptake of the drug. In other words, SJW seems to aid enzymes in the liver that inactivate and help remove drugs from the body. People taking the herb eliminate drugs from their systems faster than they otherwise would, decreasing drug levels in the blood. This is simply enhances the effectiveness of a natural

protective function of the body. It helps to prevent the suppression of the immune system. "Except for certain patients, isn't that a good thing?" Many common foods and drinks also support the cytochrome P450 enzyme system. Robert Roundtree, M.D., points out that only low numbers of people were involved in the samples for interactions between various drugs and SJW. The effect may be real, but he does not see why that makes SJW 'dangerous.' In reality, SJW has an "excellent safety record."

Herb-drug interactions are frequently in the news these days. Such interactions "are not due to any inherent toxicity of herbs." Actually, as pharmacist and naturopathic physician Michael Smith points out, herb-drug interactions occur much less frequently than predicted. And the culprits are usually the drugs, not the herbs. The German Commission-E finds SJW safe during pregnancy and lactation (nursing). But hypericin – the separated chemical – is a mild uterine stimulant, so should be discontinued if there is any spotting or cramping.

As is true with any herb, the whole form is more valuable. James A. Duke, Ph.D., recommends the dried herb taken as a tea. Varro Tyler, Ph.D., dean and professor emeritus of pharmacognosy (natural product pharmacy) at Purdue University suggests one or two cups of tea a day for four to six weeks. He explains that different chemical compounds in SJW work together to relieve depression in several different ways. The combined action of all the natural constituents also means fewer (if any) side effects because the total response is not due to a single strong action. It is naturally balanced and allows for selective absorption and biochemical individuality. [iii]

However, just as depression is not a deficiency of Prozac, neither is it a deficiency of St. John's wort. Numerous other factors must be considered. There are many possible causes of depression and many possible therapeutic approaches. Some of these will be covered in Part II of this article.

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