

St John's wort as an antidepressant

Longer term studies are needed before it can be recommended in major depression

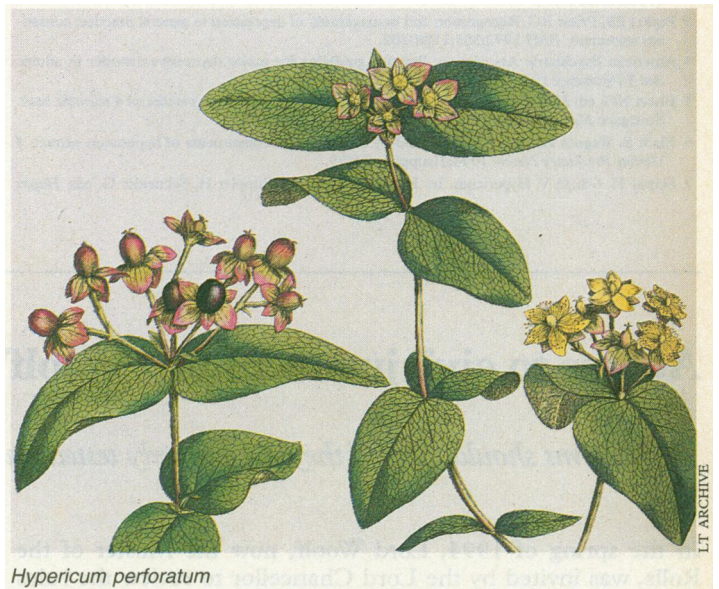
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Among the many remarkable differences between German and British medicine is the extensive use of herbal medicines in Germany. An example is the use of *Hypericum perforatum* (St John's wort) for psychological complaints. In 1994 German physicians prescribed almost 66 million daily doses of preparations containing *hypericum* alone, worth a total of DM61m (£26m).¹ In this issue Linde *et al* (p 253) conclude from a meta-analysis that hypericum extracts are more effective than placebo for treating mild to moderately severe depressive disorders.² How should this evidence be weighed?

Diagnostically, depressive disorders form a heterogeneous group which includes major depression as well as depressive states not satisfying the criteria for the full syndrome. These diagnostic types are defined not by severity but by clusters of symptoms and by the length of time they last. Since the efficacy of antidepressants in major depression is well documented, this syndrome is useful when considering treatment with antidepressants. Antidepressant drugs are particularly recommended for moderate and more severe forms of major depression.^{3 4}

One reason why German physicians may prescribe so many herbal medicines is because they are easily available. Marketing authorisation for hypericum extracts and other crude herbal medicines is obtained in Germany by reference to special phytotherapeutic monographs. When the monograph on St John's wort came out in 1984 it identified the constituent hypericin as an experimental monoamine oxidase inhibitor and permitted the medicinal use of the herb in average daily doses of 2-4 g of drug, or 0.2-1.0 mg total hypericin, for psychogenic disturbances, depressive states, anxiety, or nervous excitement.⁵ However, the clinical relevance of the monoamine oxidase inhibiting properties of hypericum extracts has not been confirmed,⁶ and hypericin is not their only bioactive constituent.⁷ Standardisation of hypericum extracts on hypericin content may therefore offer no guarantee of pharmacological equivalence.

To be accepted as an antidepressant in the strict sense—that is, to be applicable in major depression—hypericum extracts should meet the same rigorous demands that have been laid down for synthetic antidepressants.⁸ The serious nature of major depression would exclude the special licensing route that has been proposed for herbs used in minor illnesses.⁹ Linde *et al* list several short term trials in which hypericum monopreparations were more effective than placebo in less severe forms of depressive disorders. The methodological quality of these studies is variable,¹⁰ and most lack diagnostic precision because they used no classification system for psychiatric disorders or only a global classification such as the



Hypericum perforatum

international classification of diseases (ICD-9).⁷ Only one research group (Hänsgen *et al*) evaluated a hypericum monopreparation in a homogeneous group of patients with a mild to moderate form of major depression according to accepted diagnostic criteria.¹¹ This study was republished in 1996 with 36 additional patients.¹² After four weeks of treatment, hypericum extract was more effective than placebo, with a relevant difference on the Hamilton depression scale.¹² Positive results were also found in another recent trial, which compared a different brand of hypericum extract with placebo for six weeks in patients with a moderate depressive episode (according to ICD-10).¹³ Whether the observers in these multicentre trials received joint training to minimise variations in rating and whether diagnoses were reached by structured interview were not documented.

Although promising, these studies are not sufficient to accept the use of hypericum extract in major depression when judged against the criteria of the European Union guidelines for regulatory evaluation of antidepressants.⁸ For example, specific studies in severely depressed patients are still missing, as are longer term studies to assess the risk of relapse and the possibility of late side effects. Of the four trials that have compared a hypericum monopreparation with a synthetic antidepressant, none lasted longer than six weeks. All tested the comparator drug in daily amounts below or at the lower end of the usual dose range, and none of the reports described

a homogeneous patient group with major depression defined by the criteria of the *Diagnostic and Statistical Manual of Mental Disorders*.⁷ Like synthetic antidepressants, hypericum extract needs two to four weeks to develop its mood elevating effects.

The herb may offer an advantage, however, in terms of relative safety and tolerability, which might improve patient compliance. So far, its extensive use in Germany has not resulted in published case reports about serious drug interactions or toxicity after overdose. In an open study of 3250 patients the most commonly noted side effects were gastrointestinal symptoms (0.6%), allergic reactions (0.5%), and fatigue (0.4%). Whether the allergic reactions could have been related to the photosensitising potential of hypericin was not investigated. The study lasted only four weeks, and laboratory values were not systematically monitored.¹⁴

All in all, it is for good reasons that Linde *et al* ask for additional studies with better delineation of participants and for

trials lasting longer than eight weeks. When future studies compare hypericum extracts with a synthetic antidepressant this comparator should be tested in therapeutic doses and the size of the trial should be large enough to detect a clinically meaningful difference.

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Access to civil justice: Lord Woolf's visionary new landscape

The reforms should work if they are properly tested and resourced

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In the spring of 1994, Lord Woolf, now the Master of the Rolls, was invited by the Lord Chancellor to review the rules for civil procedure and to produce one rule book to replace the existing two for the high and county courts. However, he persuaded Lord Mackay of the need for a wide ranging review of the civil justice system, and has spent two years putting together his vision, aided by a panel of assessors.

Lord Woolf's final report was published last week.¹ It has been welcomed by consumers, lawyers, and by the Lord Chancellor, which should mean that this report, unlike many of its predecessors, will gradually be implemented. Lord Woolf wants to replace the present Rolls Royce system of civil justice, which has remained largely unchanged for 100 years, with a less adversarial, faster, cheaper, more affordable system. His agenda is to put clients very firmly first. He particularly wants to help ordinary citizens and small businesses to pursue or defend claims, especially against well resourced opponents.

The main planks of the proposed reforms are, firstly, the establishment of a new fast track for straightforward cases of claims under £10 000. The procedures will be simple, with clear, fixed timetables for trial within 30 weeks, and fixed costs to be paid by the losing to the winning party. When deciding whether to proceed, potential litigants should have a much better idea than now of the costs they might have to pay if they lose the case.

Secondly, more active management of larger cases by judges. Case management conferences will be held, which the clients will attend, to plan the litigation, narrow down the issues, encourage settlement, and if necessary organise the trial. A particularly important role for the judges at these con-

ferences will be to "level the playing field" when opposing parties have very different amounts of resources.

Thirdly, a range of measures to encourage openness, co-operation, and earlier settlements, including protocols of steps to be taken before proceedings are issued, pre-action discovery to be available in other cases than personal injury, positive encouragement by the courts to use mediation and other methods in appropriate cases, and the introduction of a plaintiff's offer to settle, with enhanced rates of interest, to parallel the defendant's present ability to make payments into court.

Fourthly, a much higher profile for civil justice, which has already begun with the appointment of Sir Richard Scott as head of civil justice. Other proposals to achieve this include a new Civil Justice Council to oversee and monitor the changes, on which litigants, consumer groups, lawyers, judges, and court staff will be represented; and more specialised judges, especially for complex cases such as medical negligence.

The open participatory style adopted so refreshingly by Lord Woolf and his team seems set to continue: the Lord Chancellor's department has already indicated that many of the working groups which have been producing the detailed proposals will be kept going. This should mean that lawyers and other court users will be able to continue to influence the reforms to make them workable.

Not that the proposals are without their problems. In particular, Lord Woolf seems reluctant for some of the major reforms to be tested by pilot studies. However, pilots will be essential if past disasters (such as automatic striking out of claims in the County Court) are not to be repeated. Also, it will simply not be possible