

Nevertheless, in this situation, with the caveat that this drug has not had the rigorous scientific trials other drugs have to undergo, and after taking the precaution of reviewing Franz as I would any other depressed patient, I would not disavise him from trying it.

I would recommend he buys the drug over the counter – it may well be the cheapest option – but I would want to ensure follow-up along the lines of other, more well established antidepressants. I would admit to him, though, that with regards to dose, duration of use and side-effects, we would learn together.

I would also agree a time period, say six months, after which if no effect was achieved, other alternatives would be tried. I would express hope as, after all, confidence in a treatment goes a long way in improving its overall efficacy.

### References

1 Linde K, Ramirez G, Mulrow C *et al*. St John's wort for depression – an overview and meta-analysis of randomised controlled trials, *BMJ*1996;313:253–258

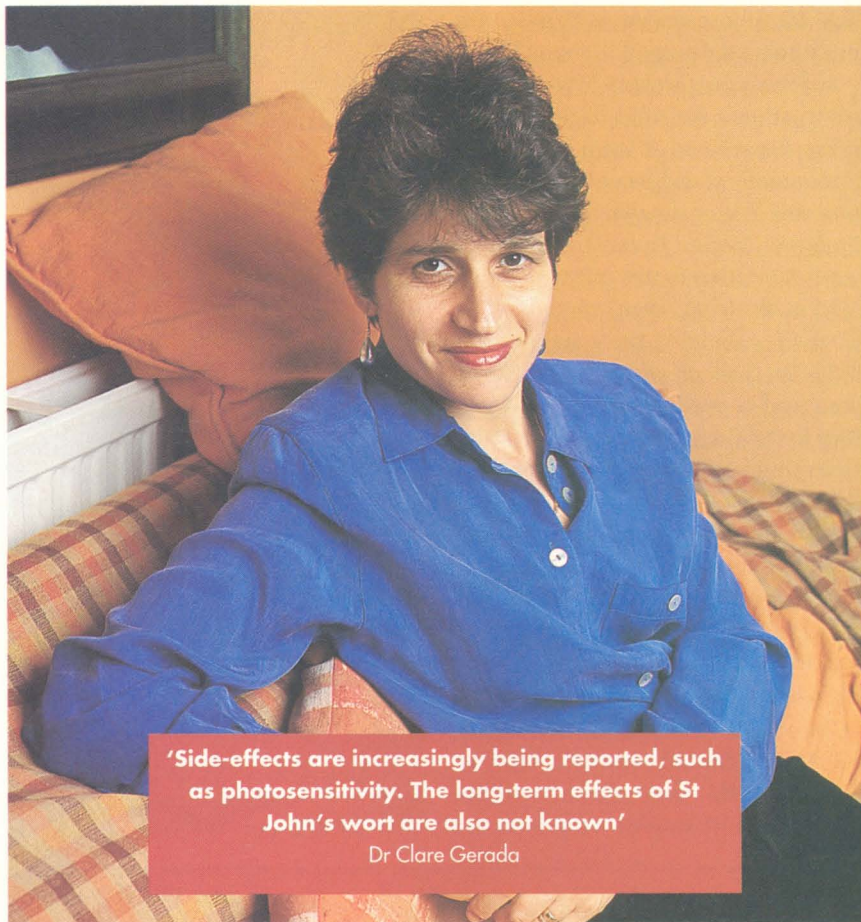
### Finally, Clinical Research Fellow **Dr Sean D Hood** examines the evidence with **Professor David Nutt** of the University of Bristol Psychopharmacology Unit:

**F**RANZ is probably right – St John's wort (hypericum) appears to be an effective treatment for mild to moderate depression. In Germany, there are more prescriptions for St John's wort each year than for the other antidepressants combined. In the UK, it is available without prescription and is increasingly popular.

St John's wort is a common perennial herb. In the Middle Ages, it was collected on St John's Day (June 25th) and soaked in olive oil, producing a red oil symbolising the blood of St John.<sup>1</sup>

The most active antidepressant compound contained by the plant appears to be hypericin. Hyperforin may also have an antidepressant effect,<sup>2,3</sup> although this constituent is usually associated with wound healing and antiseptis.

We don't really know how it works. Reports suggesting that it is a MAO



'Side-effects are increasingly being reported, such as photosensitivity. The long-term effects of St John's wort are also not known'

Dr Clare Gerada

inhibitor (like phenelzine) have not been confirmed.<sup>4</sup> One study suggested that it inhibits serotonin, dopamine and noradrenaline uptake.<sup>5</sup>

The side-effect profile has not been studied extensively, and under-reporting is likely because the myth that herbal remedies are natural and always safe will often prevent an association from being made. Also, side-effects may not be reported to the doctor, and if it does reach the doctor it may not then reach the authorities.

Nevertheless, the side-effect profile appears to be less than other antidepressants, with 4.1 per cent reporting at least one adverse reaction in placebo-controlled trials, and 19.8 per cent in trials comparing with active drugs.<sup>6</sup> The most frequent side-effects are allergic reactions, fatigue, restlessness, dry mouth and gastrointestinal symptoms.<sup>7</sup> There is no evidence that it is dangerous in overdose,<sup>8</sup> and it does not seem to impair driving or interact with alcohol.

There are potentially serious side-effects, but these are rare. An increase in theophylline levels has been reported after stopping St John's wort, suggesting caution in patients taking this and other CYP1A2 substrates such as warfarin, clozapine, olanzapine, and imipramine.<sup>9</sup> Although a reversible photosensitivity neuropathy has been reported<sup>10</sup> and has been observed in grazing animals, at normal doses this is extremely unlikely.<sup>8</sup> There is a case report of mania occurring in a patient who was also taking sertraline.<sup>11</sup>

St John's wort should be avoided in women who are pregnant or breastfeeding (two normal pregnancies have been reported<sup>12</sup>) or children, due to lack of information in these groups. It should not be co-prescribed with other antidepressants until more is known about its action, and it should be not be used to treat severe depression.

Is there solid scientific evidence of its efficacy? In recent well conducted ➤



double-blind trials, hypericum was shown to be more effective than placebo,<sup>6,13</sup> as effective as maprotiline<sup>14</sup> and imipramine<sup>15</sup> with less side-effects in the treatment of mild to moderate depression. There are other major trials in the USA currently underway.

Dosing is difficult, as St John's wort is not subject to the stringent quality controls of licensed medications, and the active constituent has not been identified. Although it has a 24-hour half-life, a bd or tds dose of 200–900mg/day is usual. Each of the double-blind studies mentioned above used a dose of 900mg/day of the Jarsin 300 brand, although I am not sure if this particular preparation is available in the UK.

Although Franz consults a practitioner for homeopathic treatments of his eczema, he has come to his GP for this medicine. This is an occasion in which it is right to tread carefully. Overemphasising the side-effects of this medication might translate as 'sour grapes' and closed-minded adherence to the traditional medical model.

Expressing openness to learn from my patient's personal experience and admitting a lack of omnipotence (taking the 'one-down' position) is a powerful manoeuvre, disarming and promoting candid discourse.

In Franz' case it would be essential to discuss the reports of phototoxicity, given his eczema, as well as considering the other issues raised above. Other possibilities such as SSRI antidepressants would be discussed to help Franz reach a balanced decision.

Although St John's wort is available without prescription, this comes at the cost of uncertain quality control. It is difficult to obtain good information about the side-effects of herbal remedies. Indeed, in a recent survey of herbal medication, 69 per cent of users said that they would not tell their GP if they had a serious adverse drug reaction associated with the remedy!<sup>16</sup> Many doctors are also not aware that since October 1996 unlicensed herbal products have been included on the UK yellow card scheme.

St John's wort is no panacea. However, it can be successfully used to



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**'The side-effect profile of St John's wort appears to be less than other antidepressants, with 4.1 per cent reporting at least one adverse reaction in placebo-controlled trials'**

Dr Sean D Hood and Professor David Nutt

treat mild to moderate depressive conditions especially in those who might not otherwise present to the GP or take conventional medicines. Rather than bury our heads in the sand, the opportunity is here for us to develop collaborative relationships with patients such as Franz, which is in all of our best interests. ■

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