

IN HIS EDITORIAL, KOOP DISCUSSES THE importance of applying scientific and regulatory tests to the use of herbal and nutritional remedies. Recent findings about St. John's wort, an herbal product used to treat a variety of ailments, including depression, raise a related issue of concern. St. John's wort has been found to interfere with the effectiveness of a wide variety of commonly used drugs (1). For example, it causes a rapid reduction in the level of the immunosuppressant



St. John's wort

cyclosporine, with attendant danger of transplant rejection (2), and a reduction in the level of an anti-HIV protease inhibitor, indinavir (3). A major ingredient of St. John's wort, hyperforin, binds to a transcription factor (the PXR protein), activating synthesis of an enzyme (cytochrome P450 3A4), which then degrades a wide variety of drugs, including not only cyclosporine and indinavir, but also the active ingredient of birth control pills. The existence of this pathway, whose normal purpose is to protect the body from noxious chemicals, is well documented in recent molecular studies (4, 5).

I agree with Koop that there may well be roles for alternative and complementary therapies in health care. It is crucial, however, that in the efforts to realize this potential, these remedies do not cause unintended damage to approved therapeutic agents.

All FDA-approved drugs are required to list precautions such as potential interactions with other drugs. It is disappointing that the bottle of St. John's wort that I recently purchased locally at a major nutritional products store contained only the most perfunctory of precautions on the label about possible interactions with drugs ("If you are taking medication, consult a healthcare professional before using this product."). Furthermore, this store was unable to provide any literature warning of possible interference with drugs.

It is noteworthy that the 2002 edition of the *Physicians' Desk Reference* (6) contains specific recommendations against co-administration of indinavir and St. John's wort and describes the interaction between

cyclosporine and St. John's wort. Given the widespread use of St. John's wort, it might be advisable for the herbal remedy and nutrition industry to provide comparable explicit warnings and information.

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#### References and Notes

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## McClintock and Marriage

AFTER READING NATHANIEL C. COMFORT'S letter about Barbara McClintock (*Science's* Compass, 18 Jan., p. 440), I feel duty bound to McClintock to relay a story that she told me in 1992 while I was researching her biography for my book *Nobel Prize Women in Science: Their Lives, Struggles and Momentous Discoveries*. In 1936, when McClintock was an assistant professor in the University of Missouri's botany department, a newspaper announced the engagement of another woman of the same name. Assuming that the engaged woman was McClintock, the department chair summoned McClintock to his office, where she was threatened with firing if she got married.



Barbara McClintock.

The University of Missouri was "awful, awful, awful," McClintock told me. "The situation for women was unbelievable, it was so bad." Eventually she was told by the dean that, if her mentor left, she would be fired. Enraged, McClintock took an immediate leave of absence without pay, with the intention of never returning. At that time, she said she never wanted another job again, and it was several years before she changed her mind.

At Cold Spring Harbor Laboratory, incidentally, McClintock could have married. Its director, Vannevar Bush, was extremely supportive of Evelyn Witkin, for example, when her children were young. McClintock never married, however, and she told me that it was because "marriage would have been a disaster. Men weren't strong enough... and I knew I was a dominant person... I knew that I'd become very intolerant, that I'd make their lives miserable."

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### CORRECTIONS AND CLARIFICATIONS

**RESEARCH ARTICLES:** "Delineation of mRNA export pathways by the use of cell-permeable peptides" by I.-E. Gallouzi and J. A. Steitz (30 Nov. 2001, p. 1895). The sequences of several of the peptides used were reported incorrectly in Fig. 1A. The actual amino acid sequences that were conjugated to AP are as follows, with substitutions indicated in bold, additions denoted by underlining, and positions of amino acids not present in the peptides used indicated by [-]: HNS: RRFGGPVHHQAQRFRFSPMGVDHMSG LSGVNPVQ; NES: [-]QLPPLRLTLD; mNES: [-]QLPDLRLTLD; and M9: NNQSSNFGPMKGGNFGGRSSG-PYGGGGQYFAKPRNQ[---]. It has been verified that the substitution of L for I [I is present in the HNS sequence of HuR; X. C. Fan, J. A. Steitz, *Proc. Natl. Acad. Sci. U.S.A.* 95, 15293 (1998)] does not alter the activity of the AP-HNS in the heterokaryon shuttling assay. Similarly, the absence of NH<sub>2</sub>-terminal N and presence of COOH-terminal GGY (as in hnRNP A1) does not alter the activity of AP-M9. The mNES sequence used and reported above is that of the well-characterized NES mutation called M10 [M. H. Malim, S. Bohnlein, J. Hauber, B. R. Cullen, *Cell* 58, 205 (1989)]; like the misrecorded mNES sequence, it differs from NES in only two amino acids. The scHNS and scM9 sequences originally reported are scrambled versions of the correct HNS and M9 sequences. Nicholas K. Conrad and Angie S. Grech are acknowledged for their work in discovering the errors and repeating the experiments.