We analyzed eight components of Chinese medicine and only Ch'an Su (Kyushin Pharmaceutical Co., Tokyo, Japan) had strong immunoreactivity, but weak reaction was also observed in the Zhu Dan component (Kyushin Pharmaceutical Co.). Digoxin-like immunoreactivity of Ch'an Su solution (10 μg/L) showed 3.88 μg/L by the Abbott TDx analyzer, 4.35 μg/L by Du Pont cca V discrete analyzer, and >5.0 μg/L (off-range) by the Enzymun-Test kit. These different values were attributed to the different cross-reactivity of antibodies to bufalin, bufotalin, and (or) cinobufagin in each method (3).

Volunteers took two tablets of Kyushin (one tablet contained 0.83 mg of Ch'an Su) three times a day, a common daily dose of this drug. In their sera, digoxin-like immunoreactivity appeared 1 h after drug intake and reached almost 0.3–0.4 μg/L within 12 h in all three methods. Cardiotoxic steroids in Ch'an Su may have weak biological activity but strong immune cross-reactivities. Therefore, patients taking both digoxin and Chinese medicine may not become actually toxic, even though they have a high, supposedly toxic value for digoxin-like immunoreactivity.

Chinese medicines are easily obtainable at common pharmacies without a doctor's prescription in Asian countries; in Japan, >300 kinds of tablets or powder contain Ch'an Su. Therapeutic monitoring of digoxin should be performed after cessation of intake of Chinese medicine.

References

Ryo Fushimi
Nobuyuki Amino

Central Lab, for Clin. Investigation
Osaka Univ. Hosp.
1-1-50 Fukushima
Fukushima-ku
Osaka 553, Japan

The author of the Letter replies:

To the Editor:

I take Fushimi and Amino's point that Ch'an Su, which contains bufadienolides, may cause problems with digoxin immunoassays; however, as I pointed out in my Letter (1), not all the digoxin assay kits I tested gave an apparent digoxin concentration after the oral intake of Lu-Shen Wan pills containing Ch'an Su. I am surprised that, in view of the 48-fold higher apparent digoxin (by Enzymun-Test) in a Ch'an Su solution as reported by Fushimi et al. (2, 3), the measured plasma concentrations of digoxin are the same by all three assays.

Ch'an Su consists of the dried secretions from the postauricular and skin glands of the toad Bufo bufo gargarizans. The resin-like secretions contain several different bufadienolides, e.g., bufalin, cinobufagin, cinobufotalin, and resibufogenin; to my knowledge, the exact components, their concentrations, and their cross-reactivities with digoxin antibodies are not known. Even amongst Lu-Shen Wan pills, there are regional preparations of the pill in China with variable contents of bufalin, cinobufagin, and resibufogenin (4). Until these Chinese medicines containing Ch'an Su are fully characterized for their bufadienolide content, one must be wary of cross-reaction problems with some of the current immunoassays for digoxin.

In the Far East the usage of herbal medicines is quite common, and preparations containing Ch'an Su are used for various ailments, including cardiac problems, as Fushimi et al. (2, 3) have stated. Rather than suggesting that "these different values [are] attributed to the different cross-reactivity of digoxin antibodies to bufalin, bufotalin, and (or) cinobufagin in each method" and advocating that patients be taken off their Kyushin tablets before therapeutic drug monitoring for digoxin, attempts should be made to identify the exact bufadienolides in these preparations and to develop specific immunoassays for them, to facilitate therapeutic drug monitoring. Such attempts may also help alleviate the phenomenon of "digoxin-like immunoreactive substance."