When I applied the common clinically used cardiac glycosides digitoxin and digoxin to leukemic cell lines, the effects were striking; potent apoptosis induction. This occurred in therapeutic plasma concentrations for treating cardiac disease. Even more intriguing was that highly proliferating normal cells were not affected at all. Digitoxin was much more potent than digoxin in these in vitro experiments. I contacted Björn Stenkvist, MD, PhD, who had reported antiancancer effects of digitals in women operated for breast cancer when taking the drug (almost all on digitoxin) due to cardiac disease. He told me that as he had done this very encouraging observation he tried to initiate studies on antiancancer effects of digitals, but there was no interest. However, when seeing the apoptosis induction in our studies, he was encouraged and made a re-analysis of the women in his study and still detected an antiancancer effect.

Now we have examined several cancer cell lines and digitoxin is a potent inhibitor of proliferation and induction of apoptosis. Recently, a group in M.D. Anderson Cancer Center confirmed our results concerning apoptosis induction in cancer prostate cells, by digitals, published earlier this year. This group has focused on a patented extract of Oleander (Anzirzel). Ralph Moss gives some of the background to Anzirzel in the excellent book, Herbs Against Cancer. Oleander contains the cardiac glycoside oleandrin that is very similar in chemical structure to digitoxin. Instead of explaining the antiancancer effects of Anzirzel with "immune-stimulating properties," an antiancancer effect of oleandrin in Anzirzel is now proposed.

We have found that the fraction of cancer cells surviving digitoxin treatment accumulate in the G2M phase of the cell cycle. Cells are more susceptible for irradiation in this phase. We also found an increased radiosensitivity in breast cancer cell lines treated with digitoxin.

Apoptosis is a very hot topic in cancer research. It is now evident that high proliferation rate is not the main problem in cancer, but impaired apoptosis. High proliferation rate of cells is normal in certain circumstances. An example is infection when immune competent cells may increase enormously and downregulate when the infectious agent is cleared away. If the apoptosis mechanisms work properly, high proliferation rate is never a problem.

Cardiac glycosides induce apoptosis in several cancer cell lines, sparing even normal cells with high proliferation rate, i.e. showing a specificity for cancer cells. They seem to work in all phases of the cell cycle. This is interesting to contrast with the observation that led to the introduction of alkylating agents in oncology in the 1940s: bone marrow and lymphoid hypoplasia in healthy people exposed to mustard gas. Since then numerous derivates of alkylating agents have been introduced. Still, the newer derivates are not specific for cancer cells but hit highly proliferating cells indiscriminately. Unfortunately, cancer cells often have a lower proliferation rate compared to the normal tissue, thus side effects are dose-limiting. It seems difficult to develop cancer specific derivates of a drug originally designed for inducing cell death in normal cells.

The in vitro data accumulated up to now show properties of the cardiac glycosides more or less perfect to treat some types of cancer. Clinical studies will reveal if this turns out to be reality.

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