This issue's topics

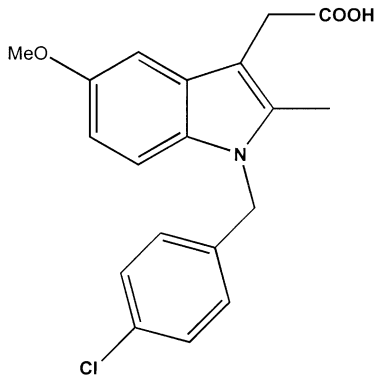

Figure of analogue 4[1]

Designer drugs

Identification of indomethacin structural homologues with potential clinical use.
By investigating the structure–activity relationships of several structural homologues of the non-steroidal anti-inflammatory drug (NSAID) indomethacin, Touhey and colleagues have identified 3 with potential clinical use. Like many NSAIDs, indomethacin can enhance the cytotoxicity of some anti-cancer drugs at non-toxic levels. The authors found that 9 of the homologues showed synergistic activity potentiating the toxicity of doxorubicin in a multidrug resistance associated protein (MRP)-expressing cell line in combination cytotoxic assays. Two of these showed no cyclooxygenase (COX)-1 and low COX-2 inhibitory activity whilst one showed low COX-1, but significant COX-2 activity, thereby making this homologue, in particular, of potential therapeutic interest due to its potential low toxicity and possible direct inhibitory effects on tumour growth. The authors state that "for certain cancers, where drug resistance is a result of MRP-1 overexpression, these active analogues are promising as potentiators of the toxicity of chemotherapeutic drugs potentially enhancing existing treatments for cancer patients".

A question of fertility?
"Will my daughter have periods after her chemotherapy?" or "Will my boy be able to father children when he is grown up?" These kinds of questions are often put to paediatric oncologists by the parents of child cancer patients after the shock of diagnosis has abated. Pubertal changes and fertility are often confused in the laymind, whereas for doctors and nurses the serial changes of treatment regimens, as protocols evolve, mean that the "target" is always moving. In addition, there is uncertainty about the possible benefits and limitations of new fertility techniques, which are evolving rapidly. The Update article by Thomson and colleagues published in this issue raises and debates some of the fertility issues. Other aspects of "late effects" are discussed in another Update by Dr. Spoudeas to be published in a later issue of the journal. There will also be further contributions to the debate in our new Update series of reviews on "Hot Topics" to be launched in the journal early next year.

Sequence-dependent synergy when ZD0473 is combined with various cytotoxics
ZD0473 is a new platinum agent that is able to overcome platinum resistance mechanisms. Rogers and colleagues have studied in this issue the treatment of 4 human ovarian carcinoma cell lines with ZD0473 alone or in combination with various cytotoxics. Cytotoxicity was assessed using the sulphorhodamine B assay. In all cell lines, paclitaxel in combination with ZD0473 demonstrated synergy. This was also seen in 3 and 2 of the cell lines in combination with the topoisomerase 1 inhibitor topotecan and anti-metabolite gemcitabine, respectively. The synergy of ZD0473 with paclitaxel was sequence-dependent, with a greater growth inhibition being observed when the cells were first incubated with ZD0473 then with paclitaxel. This was particularly marked for a cisplatin-resistant cell line, A2780CisR. At present, the mechanism is unclear.

[1] Figure provided by Dr. O'Connor and reproduced with kind permission from the authors.

Forthcoming Papers

Current Perspective
Dosing strategies for anticancer drugs: the good, the bad and body-surface area
A. Felici, J. Verweij, A. Sparreboom

Reviews
Farnesyl transferase inhibitors as anticancer agents