Non-Steroidal Antioestrogens

Molecular Pharmacology and Antitumour Activity

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1. Non-Steroidal Antioestrogens: Molecular Pharmacology and Antitumour Activity
   R.L. SUTHERLAND and V.C. JORDAN (Eds)

2. Nucleosides and Cancer Treatment: Rational Approaches to Antimetabolite Selectivity and Modulation
   M.H.N. TATTERSALL and R.M. FOX (Eds)

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This book is dedicated to the memory of Dr A. L. Walpole

Preface

It is now more than twenty years since the first report of an effective non-steroidal antioestrogen, MER 25, was published. This original work inspired many research groups to synthesize and test related compounds as potential antifertility agents. However, the only compounds to reach the clinic (clomiphene and tamoxifen) proved to be inducers of ovulation and are now used routinely in sub-fertile patients.

The work by Dr Elwood V. Jensen and others, which suggested some human breast cancers were directly dependent on oestrogen, led to the initiation of clinical trials with synthetic antioestrogens. Encouraging preliminary results with nafoxidine were offset by a high incidence of troublesome side-effects. However, the successful introduction of tamoxifen for the treatment of advanced breast cancer has resulted in a renewed interest in the pharmacology and mechanisms of action of these drugs.

The exponential increase in the number of research articles on anti-oestrogenic mechanisms throughout the 1970s prompted us to attempt to summarize the wealth of available data in a single volume. As a basis, much of the information published in this book was presented at an Antioestrogen Workshop held at the Ludwig Institute for Cancer Research, University of Sydney, Australia between the 4th and 6th February, 1980. Due primarily to limitations of space we have only been able to include those areas of antioestrogen research that relate to the development and action of antioestrogens as anticancer agents. For this reason a substantial literature on the effects of antioestrogens in reproductive and behavioural biology has not been included.

The untimely death of Dr Arthur L. Walpole in 1977 unfortunately did not allow him to witness the world-wide acceptance of tamoxifen as an effective

therapy for advanced breast cancer. Tamoxifen was developed by Drs M. J. K. Harper, D. Richardson and A. L. Walpole as part of the fertility control programme at Imperial Chemical Industries Ltd, Pharmaceutical Division, but it was Dr Walpole's deep interest in cancer research that led to its ultimate introduction as an antitumour agent. On a personal note, Dr Walpole was known as a scientist who helped and encouraged young investigators,including one of the editors of this volume (V.C.J.). It is for these reasons that we have dedicated this volume to his memory.

The keen interest shown by the UICC, Imperial Chemical Industries Ltd, Eli Lilly and Co. and Upjohn Pty Ltd in both the Antioestrogen Workshop and the preparation of this volume is gratefully acknowledged.

Finally we would like to thank Christine Cook, Elaine Heffernan, Leigh Murphy, Anne Whybourne, Terry Foo, Mike Green, Roger Reddell and Colin Watts without whose help this venture would not have been possible.

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