

SALICYLATES

An International Symposium

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With 43 Figures and 8 Plates

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SALICYLATES

An International Symposium

PREFACE

THIS symposium was the first occasion on which were gathered together those specifically interested in the salicylates. The variety of topics discussed and the different scientific disciplines represented at the meeting reflected the impact of these relatively simple drugs on many fields of research. The salicylates possess serious claims to scientific attention because they are among the most ancient of remedies and yet have stood the test of time, because they have a remarkable resilience as chemotherapeutic agents, and because of the range and diversity of their useful and toxic actions.

During the eighty years since the introduction and widespread use of synthetic preparations a voluminous literature has accumulated. Nevertheless it has not been possible to formulate precise ideas either about the mode of action of salicylates or to explain the exact manner in which they produce their toxic effects. It was hoped that this meeting would provide the opportunity to take stock of our present knowledge and thus to focus attention on those aspects that seemed of importance for future advances in this field.

Under the sponsorship of the Empire Rheumatism Council, with the support of the Nicholas Research Institute Ltd., the main responsibility for the meeting lay in the hands of an Organizing Committee, who have also acted as the Editorial Committee for this report. The Committee is grateful to the Postgraduate Medical School of London for the excellent facilities made available at the Wolfson Institute, and to the Arthritis and Rheumatism Foundation of America and to a number of pharmaceutical companies for grants for travelling expenses for some of the overseas participants. The Committee is also indebted to the Nicholas Research Institute Ltd. for a subsidy towards the costs of production of this report.

The proceedings of the symposium have been edited in order to present the material in a form more suitable for publication as a book. It is hoped also that the report may serve as an up-to-date bibliographic review of the subjects discussed. The committee have endeavoured to see that full references are cited. Where no reference is quoted, the inference to be drawn is that the work has not been published. Where work is referred to in the discussions by the author's name only, the full reference will be found in the bibliography at the end of the papers immediately preceding that discussion. Reference to work mentioned during the symposium is made only by designation of the author's name in capital letters; page references are not given, but can be found easily from the Contributor Index. When reference is made to the work

of someone who happened to be present but who had not presented this work at the symposium, this convention does not apply.

In general the use of proprietary names has been avoided, although if the proprietary name is used it is treated as a proper noun. Preference has been given to B.P., B.P.C., or Approved Names, or to standard chemical nomenclature. The only instance in which this nomenclature may not be universally understood occurs with Paracetamol, the chemical name of which is *N*-acetyl-*p*-aminophenol (Acetaminophen, U.S.A.N.). For proprietary products that were referred to frequently we have used certain synonyms that most people already understand:

Disprin and Solprin (Reckitt & Sons Ltd.).	soluble aspirin
Bufferin (Bristol-Myers Company)	buffered aspirin
Alka-Seltzer (Miles Laboratories Ltd.).	effervescent aspirin
Paynocil (Beecham Research Laboratories Ltd.).	aspirin-glycine
Calurin (Dorsey Laboratories)	calcium aspirin urea
Enseal and Nuseal coatings (Eli Lilly & Company Ltd.)	enteric-coated aspirin or sodium salicylate (unless coating specified otherwise)
Trafuril (Ciba).	thurfyl nicotinate cream

These terms are used with these specific meanings in the singular; when used in the plural their meaning is more general, e.g. soluble aspirins include any preparation that is dissolved readily in water.

The Committee is indebted to Miss Beryl Howard and Miss Pamela Coates for much assistance, to Messrs. Harry Cooper for transcribing the proceedings of the symposium, to Miss D. F. Atkins for checking the references, and to Mr. David Banks for redrawing most of the figures. The Committee also wish to thank Mr. M. C. G. Andrews, General Secretary of the Empire Rheumatism Council, for his support and help.

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INTRODUCTION

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As Chairman of the Empire Rheumatism Council, which has helped to sponsor this meeting, it is my pleasant duty to welcome you here today. Those who know our Council will forgive me if I remind others that it is the body which, above others in this country, has put the subject of rheumatology on the map in the past 25 years. Its objects are to foster research into all aspects of rheumatic diseases. The Council also encourages teaching, both lay and medical, within this field, and it tries to stimulate such public authorities as are susceptible to stimulation to provide better treatment both in this country and in the Commonwealth. One of the Council's more recent activities has been sponsoring symposia such as this. We have organized six so far, the subjects including genetics, auto-immunity, and certain aspects of orthopaedics. Symposia are always arranged by invitation and therefore the people who are wanted are present. I believe I am right in saying that we have practically never so far had a refusal from anyone whom we have invited. I think, therefore, that the workers in these various fields must feel that these symposia form a useful contribution.

The idea, of course, is to bring together workers in a specified field who might not otherwise have these contacts, and today there are assembled clinicians, medical men engaged in research, and pharmaceutical experts, some qualified medically and some not.

I am sure that you are not under the delusion that the salicylates form a new subject. I should like to remind you that the great Thomas Sydenham, who was called the English Hippocrates, in the seventeenth century initiated the fashion for the barks of trees as sources for medicinal compounds because the Peruvian or Jesuit's bark, which yielded quinine, had just been introduced and found to be of great medicinal use in an England where malaria was still endemic. Consequently barks of indigenous trees were explored, including the genus *Salix*. The barks of the willow and poplar trees were found to yield a substance which was an antipyretic and useful as a bitter—and bitters were popular in those days for medicinal purposes. (Until the world-shattering invention of angostura bitters, during the last century, the poplar bark was also used for flavouring drinks, salicin being the active principle—as quinine is, I believe, of its successor.)

Then in 1838 Piria discovered salicin and in 1876, in the lifetime of

people still living, this was used for the treatment of rheumatic disease by Maclagan of Glasgow. Next year the German Professor, Senator, suggested that salicylic acid, which had recently been synthesized, might prove less irritant. This was found to be so, and that was the real beginning of salicylate therapy as we know it today.

This may well prove to have been an historic assembly from the point of view of this subject, which has not previously been discussed in its entirety by experts. It is a pleasure to welcome Professor Niederland from Czechoslovakia, Professor Domenjoz from Germany, Dr. Wilhelmi from Switzerland, Dr. Kelemen from Hungary, Professor van Cauwenberge from Belgium, and Dr. Stubbé from The Netherlands, in addition to a number of distinguished workers from the United States. I feel sure that you will advance knowledge, and I hope that you will have a pleasant three days.