
Preface

Histamine [2-(4-imidazolyl) ethylamine] is a biogenic amine that is synthesized from the amino acid L-histidine through the catalytic activity of histidine decarboxylase (HDC, EC 4.1.1.22) and catabolized by two enzymes, namely diamine oxidase (DAO, EC 1.4.3.6) and histamine N-methyltransferase (HNMT, EC 2.1.1.8) [1, 2].

The history of histamine and antihistamines reflects numerous pioneering moments in the development of pharmacology over the last 100 years, achieved by research groups led by outstanding scientists, including six Nobel Prize winners: Paul Ehrlich, Charles Richet, Adolf Windaus, Sir Henry Dale, Daniel Bovet, and Sir James Black (Fig. 1).

Histamine was chemically synthesized by Adolf Windaus and Karl Vogt in 1907 [3], and the investigation of its pharmacological actions started in the early twentieth century by Sir Henry H. Dale in the Wellcome Research Laboratories in south-east London [4]. One of the first described actions of histamine was its ability to mimic the anaphylactic reaction [4]. A few years earlier, Paul Portier and Charles R. Richet had coined the term “anaphylaxis” [5] and Clemens von Pirquet and Bela Schick the term “allergy” to describe the hypersensitivity reactions [6]. However, it was not until the early 1950s that James Riley and Geoffrey West associated histamine with the mast cell [7] which had been discovered more than 70 years earlier by Paul Ehrlich [8] and was linked to anaphylactic reactions in 1941 [9].

In addition to its pivotal role in hypersensitivity reactions [10], smooth muscle contraction [11], and vascular permeability [10, 12], we now know that histamine is produced and released from a variety of cells and modulates gastric acid secretion [13], neurotransmission [14], and immune cell chemotaxis [15]. Its regulatory properties are mediated through four types of G protein-coupled receptors (GPCR), designated as H₁, H₂, H₃, and H₄ [16, 17] which are differentially expressed in various tissues and cell types and show intra- and interspecies variations [18]. In general, the tissue distribution and localization in target cells associate the H₁, H₂, H₃, and H₄ receptors with allergy, gastric acid secretion, neurotransmission, and immunomodulation, respectively [15–18].

For more than 70 years, histamine has been one of the most exploited substances in medicine (Fig. 1). It has provided blockbuster drugs acting on H₁ and H₂ receptors for the treatment of allergies and gastrointestinal disorders, respectively. Interestingly, the high affinity H₄ receptor was identified in 2000, and since then it has been shown to be constitutively active and expressed mostly, but not exclusively, on cells of the immune system. This discovery revealed novel attractive perspectives for the translational potential of this new drug target in acute and chronic inflammation, autoimmune disorders, host defense, and neuropathic pain. Histamine also has profound effects in cancer. Claude Burtin found that cimetidine increased the survival of patients with advanced cancer [19]. However, the pharmacological diversity and complexity of histamine receptors (HRs) and their ligands, as well as their association with the recently described phenomenon of “biased agonism,” justifies ongoing efforts to translate preclinical drug actions into promising therapies for pathologies with high economic and societal impact, such as asthma, dementias, dermatitis, and arthritis.

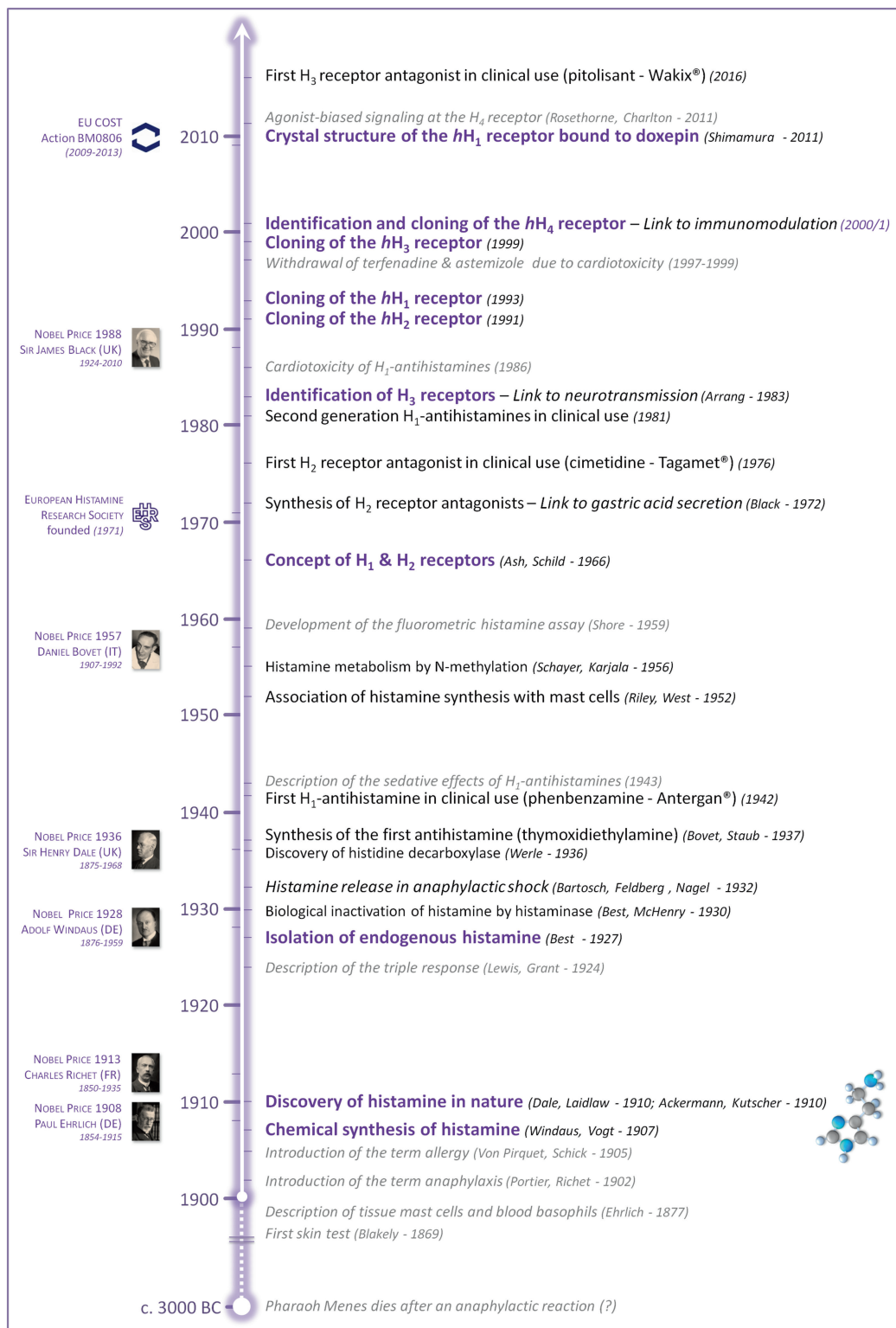


Fig. 1 Milestones in the pharmacology and the therapeutic exploitation of histamine and histamine receptors (H₁–H₄)

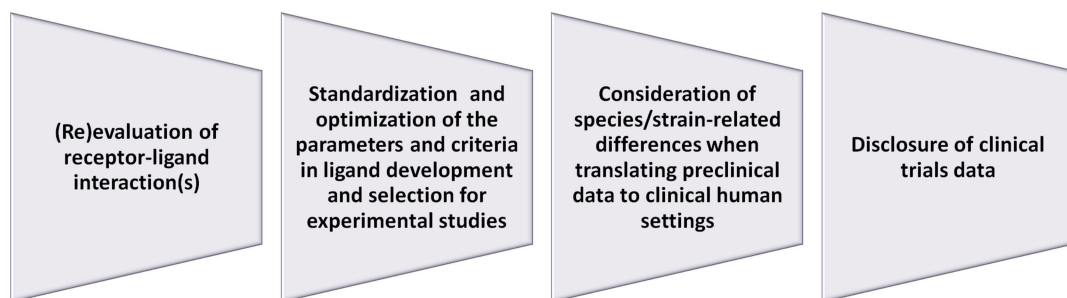


Fig. 2 Key perspectives directing future histamine and histamine receptor research towards the development of new drugs

This book illustrates the current state of the art in histamine research. It is designed to comprehensively present the most effective methods and protocols available in order to aid researchers around the world in pursuing the study of this vital scientific area (Fig. 2). It largely focuses on the appropriate methodologies to investigate the pharmacological properties and the therapeutic exploitation of HRs and their ligands. In addition, the range of techniques described in this volume also provides an introduction to complementary cross-methodological disciplines beyond these fields. This multidisciplinary approach is required to define the “decision gates” that determine the development of more effective and safer therapeutic options for many forms of highly prevalent and debilitating diseases.

Chapters that deal with critical discussions on both laboratory and clinical topics have mainly been contributed by members of the long-standing European Histamine Research Society (EHRS). In general, chapters contain an informative theoretical part and a detailed methods section, all supported by extensive bibliography. The aim is to help academic and industry drug discovery researchers and pharmacologists to deliver beneficial end points through basic and translational research (Fig. 2). The target audience includes pharmacologists, biochemists, drug discovery researchers, molecular biologists, chemists, toxicologists, lab scientists, medical doctors, principal investigators, research scientists, lab directors and technicians, as well as graduate students.

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