Preface

Capsaicin, a homovanillic acid derivative (8-methyl-N-vanillyl-6-nonenamide), is the pungent ingredient in red peppers of the plant genus *Capsicum*, including chillies and jalapenos. Capsaicin has long been used as a probe for sensory neuronal mechanisms. This is because capsaicin selectively stimulates, and at large doses, defunctionalizes a subset of primary afferent neurons with unmyelinated C fiber or thinly myelinated Aδ fibers. Most capsaicin-sensitive fibers are polymodal nociceptors (which respond to a range of sensory stimuli including noxious heat, pressure, and chemical irritation) as well as heat nociceptors, mechano-heat insensitive chemonociceptors, and warm receptors. The molecular site of action of capsaicin and other structurally related substances have been identified and cloned. This receptor, the transient receptor potential vanilloid 1 (TRPV1), formerly vanilloid receptor subtype 1 (VR1), forms a nonselective cation channel in the plasma membrane that is highly expressed in peripheral and central terminals of these primary sensory neurons. Capsaicin application at submicromolar concentrations activates the subset of polymodal nociceptor fibers that express its receptor; this leads to release of neuropeptides, such as substance P and calcitonin gene-related peptide, from nerve terminals and burning pain. Higher concentrations or the repeated application of low concentrations of capsaicin leads to desensitization, i.e., decline in response to capsaicin and also to other stimuli of polymodal nociceptors. This desensitizing action has made capsaicin attractive for use as a peripherally acting analgesic for chronic painful syndromes.

Capsaicin has moved toward clinical applications and is used currently in topical creams and gels to relieve intractable neuropathic pain, uremic pruritus, and rheumatoid arthritis. Capsaicin also proved of value in nonallergic (vasomotor) rhinitis, migraine, cluster headache, herpes zoster, and bladder overactivity and interstitial cystitis. Resiniferatoxin is an ultrapotent capsaicin analog isolated from the dried latex of the cactus-like plant *Euphorbia resinifera*. In patients with overactive bladder, intravesical resiniferatoxin improves bladder function without having significant irritancy and/or toxicity. Intrathecal resiniferatoxin is currently undergoing clinical trials in patients with intractable cancer pain. Capsaicin and capsaicin-like molecules have thus remarkable potential as pharmaceutical agents for treating various human ailments.

The intended purpose of this volume is to compile the available knowledge and the most recent achievements pertaining to the application of capsaicin and
capsaicin-like molecules in the management of various human ailments. It also
seems timely to cover basic issues on the capsaicin receptor, the mechanisms of
its action, and its role in physiological and pathological processes and provide the
latest perspectives on these issues. The book aimed to combine both basic
science on the pathophysiological role of sensory nerves and TRPV1 in the
disease process itself, in addition to covering current knowledge and highlighting
the most recent progress in the use of capsaicin as a therapeutic agent. Each
chapter is written by noted experts in their field of endeavor. In this way, it is
hoped that the book will be useful for both clinicians and researchers and that it
will stimulate their future research.

I would like to thank all the authors of this volume who worked diligently to
produce such outstanding chapters that not only covered current knowledge but
also discussed important potential pharmaceutical implications for further research
in this field. This book has been only possible because of their efforts. I am most
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