

Preface

Gastrointestinal cancers account for more than one third of all deaths from cancer. Peritoneal dissemination is considered as an advanced stage in the natural history of these malignancies and a frequent finding in the recurrent condition. As a curative approach to peritoneal surface malignancies confined to the peritoneal cavity, cytoreductive surgery combined with perioperative intraperitoneal chemotherapy has brought about long-term benefits in selected patients with peritoneal carcinomatosis (PC) of gastrointestinal origin and pseudomyxoma peritonei (PMP) syndrome. However, intraperitoneal chemotherapy fails to maintain the surgical complete response in a proportion of patients with gastrointestinal PC and PMP. In this context, mucins aberrantly expressed by tumor cells are believed to play key roles in tumor biology and pathogenesis, contributing to the tumor growth and progression, resistance to chemotherapy, evasion of immune surveillance, and formation of mucinous ascites.

While providing the reader with a detailed overview of peritoneal surface malignancies and an in-depth understanding of the role of mucin in the pathogenesis of mucin-producing tumors, this monograph introduces a novel locoregional approach to these challenging entities. This experimental treatment is capable of enhancing microscopic cytoreduction, eliminating mucin, and maximizing cytotoxic effects of chemotherapeutic agents on tumor cells while minimizing their toxic effects on host cells. Such a treatment has thus the potential to improve therapeutic benefits of the current multidisciplinary strategies in patients with mucin-producing peritoneal malignancies. The first chapter outlines the classification of peritoneal surface malignancies and discusses gastrointestinal PC as well as PMP syndrome. Each section describes the incidence and natural history of the disease, pathogenesis, predicting and predisposing factors, diagnostic and prognostic evaluation, and the state-of-the-art treatment. Results from studies using cytoreductive surgery and perioperative intraperitoneal chemotherapy along with pros and cons of this curative approach are summarized at the end of each section. The second chapter introduces the diverse family of mucin glycoproteins with emphasis on their classification, regulation, and role in health and cancer. This is followed by two chapters devoted to bromelain and *N*-acetylcysteine, the two natural agents used in our experimental

treatment. These chapters include a brief history of the evolution of the drugs over the past decades and provide an overview of their biochemical properties, pharmacokinetics, pharmacodynamics, potential and actual applications, safety, and tolerability. Of particular interest are their potential benefits in the management of cancer that have been reviewed in further detail. Eventually, the last chapter summarizes our findings on the combined use of bromelain and *N*-acetylcysteine in treating the experimental models of gastrointestinal PC and PMP, indicating (a) inhibitory effects on malignant cell and tumor growth; (b) chemosensitizing effects on cancer cells treated with commonly used chemotherapeutic agents; and (c) mucin-depleting effects observed as a decrease in mucin produced/secreted by cancer cells both in vivo and in vitro.

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Utility of Bromelain and N-Acetylcysteine in Treatment of
Peritoneal Dissemination of Gastrointestinal
Mucin-Producing Malignancies

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