AAP Research Notes in Chemistry **Medicinal Chemistry** with Pharmaceutical **Product Development** Editors Debarshi Kar Mahapatra Sanjay Kumar Bharti APPLE ACADEMIC PRESS

Apple Academic Press Inc. 3333 Mistwell Crescent Oakville, ON L6L 0A2 Canada

Apple Academic Press Inc. 1265 Goldenrod Circle NE Palm Bay, Florida 32905 USA

© 2019 by Apple Academic Press, Inc.

Exclusive worldwide distribution by CRC Press, a member of Taylor & Francis Group

Exclusive worldwide distribution by CRC Press, a member of Taylor & Francis Group

No claim to original U.S. Government works International Standard Book Number-13: 978-1-77188-710-6 (Hardcover)

International Standard Book Number-13: 978-0-42948-784-2 (eBook)

International Standard Book Number 1998
Intern All rights reserved. No part of this work may be reprinted invented, including photocopying or by any electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or hereafter invented, including photocopying and re-electric, mechanical or other means, now known or necessary in the re-electric mechanical or other means, now known or hereafter invented, including photocopying and re-electric mechanical or other means, now known or hereafter invented in the re-electric mechanical or other means are re-electric mechanical or other means and re-electric mechanical or other mech All rights reserved. To photocopying and receptive, mechanical or other means, now known of fleethic, mechanical or other means, now known of fleethic, mechanical or other means, now known of fleethic mechanical or other electric, mechanical of the published or retrieval system, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, or in any information storage or retrieval system, cording, cordinate cording, cordinate cordinat

er or its distributor, except in the case of This book contains information obtained from additional additional actions and sources are indicated. Copyright for individual articles remains with the quoted with permission and sources are listed. Reasonable efforts have been made to be the publisher cannot seem and the pu This book contains and sources are indicated. Copy Reasonable efforts have been made to with the authors as indicated. A wide variety of references are listed. Reasonable efforts have been made to publish the authors as indicated. A wide variety of references are listed. Reasonable efforts have been made to publish the authors as indicated. A wide variety of references are listed. The authors editors authors as indicated. A wide variety of references are fisted authors as indicated. A wide variety of references are fisted authors as indicated. A wide variety of references are fisted authors, and the publisher cannot assume responsibility for reliable data and information, but the authors, editors, and the publisher for the consequences of their use. The authors, editors, and the publisher for the publisher for the consequences of their use. reliable data and information, but the authors, editors, data and information, but the authors, editors, and the publisher for the validity of all materials or the consequences of their use. The authors, editors, and the publisher for the validity of all materials or the convergence of all material reproduced in this publication and application and application. the validity of all materials or the consequences of their decreption and apologize to attempted to trace the copyright holders of all material reproduced in this publication and apologize to attempted to trace the copyright must be attempted attempted to trace the copyright holders of all material representation and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material copyright holders if permission to publish and let us know so we may rectify in any future reprint copyright holders if permission to put has not been acknowledged, please write and let us know so we may rectify in any future reprint.

has not been acknowledged, predation has not bee and identification without intent to infringe.

Library and Archives Canada Cataloguing in Publication

Medicinal chemistry with pharmaceutical product development / edited by Debarshi Kar Mahapatra, PhD, Sanjay Kumar Bharti, PhD.

(AAP research notes on chemistry)

Includes bibliographical references and index.

Issued in print and electronic formats.

ISBN 978-1-77188-710-6 (hardcover).--ISBN 978-0-429-48784-2 (PDF)

1. Drug development. 2. Pharmaceutical chemistry. I. Mahapatra, Debarshi Kar, editor II. Bharti, Sanjay Kumar, editor III. Series: AAP research notes on chemical engineering

RM301.25.M43 2018

615.1'9

C2018-906021-2

C2018-906022-0

Library of Congress Cataloging-in-Publication Data

Names: Mahapatra, Debarshi Kar, editor. | Bharti, Sanjay Kumar, editor.

Title: Medicinal chemistry with pharmaceutical product development / editors,

Debarshi Kar Mahapatra, Sanjay Kumar Bharti.

Description: Toronto; New Jersey: Apple Academic Press, 2019. | Series: AAP research notes on chemistry | Includes bibliographical references and index.

Identifiers: LCCN 2018049885 (print) | LCCN 2018050211 (ebook) | ISBN 9780429487842 (ebook) | ISBN 9781771887106 (hardcover)

Subjects: | MESH: Chemistry, Pharmaceutical

Classification: LCC RM301.25 (ebook) | LCC RM301.25 (print) | NLM QV 744 |

DDC 615.1/9--de23

LC record available at https://lccn.loc.gov/2018049885

Apple Academic Press also publishes its books in a variety of electronic formats. Some content that appears in print may not be excited. in print may not be available in electronic format. For information about Apple Academic Press products, visit our website at a product of the product of th visit our website at www.appleacademicpress.com and the CRC Press website at www.crcpress.com

CONTENTS

7.

	About the Editorsxi	
	Contributorsxiii	
	Abbreviationsxv	
	Prefacexxi	
	Forewordxxii	i
	1. Protein Function as Cell Surface and Nuclear Receptor in Human Diseases Urmila Jarouliya and Raj K. Keservani	1
2	2. Islet Transplantation in Type 1 Diabetes: Stem Cell Research and Therapy Parveen Parasar and Vivek Singh	33
3.	Novel Anti-Cancer Drugs Based on Hsp90 Inhibitory Mechanisms: A Recent Report	57
4.	Nanosuspensions as Nanomedicine: Current Status and Future Prospects	105
5.	Nanocarrier Technologies for Enhancing the Solubility and Dissolution Rate of API Ashwini Deshpande and Tulshidas S. Patil	155
6.	Recent Perspectives of Chalcone-Based Molecules as Protein Tyrosine Phosphatase 1B (PTP-1B) Inhibitors Debarshi Kar Mahapatra, Sanjay Kumar Bharti, and Vivek Asati	235
7.	Briefing Therapeutic Approaches in Anticoagulant,	
	Thrombolytic, and Antiplatelet Therapy	253
	Kuntal Manna and Manik Das	

x		Contents
8.	Insulin Therapy for Diabetes: Current Scenario and Future Perspectives	
	Yogesh A. Kulkarni, Mayuresh S. Garud, and R. S. Gaud	293
9.	Emerging Potential of In Vitro Diagnostic Devices:	
	Applications and Current Status Swarnali Das Paul and Gunjan Jeswani	319
Inde	ж	35

RECENT PERSPECTIVES OF CHALCONE-BASED MOLECULES AS PROTEIN TYROSINE PHOSPHATASE 1B (PTP1B) INHIBITORS

DEBARSHI KAR MAHAPATRA, SANJAY KUMAR BHARTI, and VIVEK ASATI

Department of Pharmaceutical Chemistry, Dadasaheb Balpande College of Pharmacy, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, Maharashtra, India

Institute of Pharmaceutical Sciences, Guru Ghasidas Vishwavidyalaya (A Central University), Bilaspur – 495009, Chhattisgarh, India, E-mail: skbharti.ggu@gmail.com

ABSTRACT

Diabetes mellitus (DM) is a heterogeneous group of disorders which is characterized by increased blood sugar level, altered metabolism of lipids, carbohydrates, and proteins and increased risk of complications from vascular disease. Protein Tyrosine Phosphatase 1B (PTP1B) has gained adequate notice due to its crucial role in type 2 diabetes (t2D) and obesity as a negative regulator of the insulin and leptin-signaling pathway. PTP-1B is primarily responsible for dephosphorylation of the insulin receptor and thus down regulates insulin signaling. PTP1B inhibitors are the latest candidate for the management of diabetes, where they prevent dephosphorylation of the insulin receptor and consequently increase insulin level. Natural products have been reported to exhibit promising anti-diabetic activity. Chalcones or 1,3-diphenyl-2*E*-propene-1-one, the open chain intermediate in aurones synthesis of flavones containing benzylideneacetophenone scaffold, where the two aromatic nuclei are joined by a three-carbon α, β

236

unsaturated carbonyl bridge have shown tremendous PTP1B inhibition. In this chapter, a concrete focus on pharmacology, mechanism of action, and structural aspects along with substituents required for modulating PTP1B has been discussed. Still, none of these inhibitors have gained adequate attention at present and need to be explored and evaluated properly in terms of efficacy and toxicity to develop as therapeutic agents/formulations for the management of diabetes in future.

6.1 INTRODUCTION

Diabetes Mellitus (DM) is a heterogeneous group of disorders which is characterized by increased blood sugar level, altered metabolism of lipids carbohydrates, and proteins and increased risk of complications from vascular disease [1]. The chronic hyperglycemic conditions are associated with dysfunction and failure of major organs like heart, eyes, nerves, blood vessels and kidneys [2]. The American Diabetes Association (ADA) defines that DM is characterized by polyuria, polydipsia, polyphagia, glycosuria, unexplained weight loss and random plasma glucose concentration of greater than 200 mg/dL along with fasting plasma glucose concentration of greater than 126 mL/dL [3]. Variations in normal glucose homeostasis occur by numerous factors like impaired insulin secretion, hepatic gluconeogenesis and reduced uptake of glucose by skeletal muscle, adipose tissues and liver [4]. In the case of type I diabetes, the body does not produce enough insulin that is required to convert sugar, starches, etc. into energy. Type II diabetes (t2D) is a condition characterized by situation where cells do not properly use insulin as a result of "resistance" [5]. The most prominent features of type II diabetes is decreased sensitivity of muscle and adipose cells to insulin. T2D is often characterized by intrinsic problems like compliance, ineffectiveness and hypoglycemic episodes with insulin and the sulfonylureas. Administration of glitazones are not effective in all t2D patients, therefore, the great need for more effective orally administered agents particularly ones that normalize both glucose and insulin levels still remains a challenge [6]. Insulin is secreted in two discrete phases from pancreatic β -cells which influence the magnitude of both facting and read as β -cells which influence the magnitude of both fasting and postprandial blood glucose concentrations. In the beginning, a rapid release of insulin occurs, when the glucose concentration