



UNIVERSITI PUTRA MALAYSIA

***MICROWAVE AND CONVENTIONAL SYNTHESIS OF NEW
DIHYDROBENZIMIDAZOQUINAZOLINE DERIVATIVES AND THEIR
BIOLOGICAL ACTIVITIES***

HIBA ALI HASAN

FS 2018 86



**MICROWAVE AND CONVENTIONAL SYNTHESIS OF NEW
DIHYDROBENZIMIDAZOQUINAZOLINE DERIVATIVES AND THEIR
BIOLOGICAL ACTIVITIES**

By

HIBA ALI HASAN

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia,
in Fulfilment of the Requirements for the Degree of
Doctor of Philosophy**

April 2018

COPYRIGHT

All material contained within the thesis, including without limitation text, logos, icons, photographs and all other artwork, is copyright material of Universiti Putra Malaysia unless otherwise stated. Use may be made of any material contained within the thesis for non-commercial purposes from the copyright holder. Commercial use of material may only be made with the express, prior, written permission of Universiti Putra Malaysia.

Copyright © Universiti Putra Malaysia



DEDICATION

To whom bears me through weakness upon weakness...
To whom her prayer lightened my path...
To the source of tenderness...
To my first teacher “**mom**”

To the most supportive man...
To the character of sacrifice and loyalty...
To whom taught me meaning of preciseness “**Dad**”

To the apple of my eye...
To my smile and absolute hope...
To whom has that kind of patience despite of her young age...
To “**Shams**”, my daughter...

To the best friends in my life
To “**Huda and Dhuha**”, my sisters and “**Al-hasan**” my lonely brother...

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

**MICROWAVE AND CONVENTIONAL SYNTHESIS OF NEW
DIHYDROBENZIMIDAZOQUINAZOLINE DERIVATIVES AND THEIR
BIOLOGICAL ACTIVITIES**

By

HIBA ALI HASAN

April 2018

Chairman : Emilia binti Abd Malek, PhD
Faculty : Science

Inspired by the biological prominence of benzimidazoquinazoline, and trying to solve bacterial resistance problem as well as imbalance of antioxidant mechanisms inside our bodies, in this study, two series of eighteen dihydro-benzimidazoquinazoline derivatives (fifteen new derivatives except **39**, **45**, and **47**) were synthesised. These two series were synthesised from the reaction of 2-(2-aminophenyl)-1*H*-benzimidazole with two different series of aliphatic and aromatic aldehydes in a single step to investigate the activities of aliphatic as well as aromatic derivatives.

The compounds were synthesized using two different techniques of traditional heating by reflux and microwave-assisted organic synthesis (MAOS). A comparative study was used to compare the efficiency of these two protocols to synthesise the same target compounds regarding the reaction time, percentage yield, purity of the compounds, and benignity towards the environment. Furthermore, the structures of eighteen compounds were confirmed by applying TLC, spectrometric analysis (1D and 2D NMR, FTIR, and GCMS), elemental analysis (CHN) and photoluminescence properties (PL). Accordingly, single crystal analysis was performed for five crystal samples for further confirmation. The *in vitro* antimicrobial and antifungal activity was assessed against a panel of bacteria and fungi: two Gram-positive (*Staphylococcus aureus* ATCC 43300 and *Bacillus subtilis* UPMC 1175), two Gram-negative (*Pseudomonas aeruginosa* ATCC 15542 and *Salmonella choleraesuis* ATCC 10708), and one fungus (*Aspergillus brasiliensis* ATCC 16404) to test their biological activity against new microorganisms. Furthermore, ABTS and DPPH antioxidant activities of these analogues were performed to investigate their scavenging activities.

The microwave-enhanced synthesis method revealed superiority over its comparable method to synthesize the same type of compounds. The investigation of the antibacterial activity for both compound series (aliphatic and aromatic) revealed that some compounds gave moderate to good ability to inhibit Gram-positive bacterial growth, while only one compound in the aromatic family resulted in excellent inhibitory activity compared to tetracyclin standard drug. Neither of the two series displayed any inhibitory activity against the Gram-negative bacteria nor fungus. The ABTS scavenging activity for both series disclosed more powerful efficiency than for DPPH, as well as some of the derivatives displayed excellent antioxidant activity for both tests.

Fifteen new compounds together with another three known derivatives were synthesized to test their biological activities. The study found that the dihydro-benzimidazoquinazolines were synthesised within minutes by only one step to produce ultra-pure fluorescent compounds with very good to excellent yields (82-98%) in a more benign method towards the environment. The antimicrobial and antioxidant activities were investigated for these derivatives whereby, some of the compounds disclosed powerful activity that may help for future drug candidate development.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

**SINTESIS BERGELOMBANG MIKRO DAN KONVENSIONAL
DERIVATIF BARU DIHIDROBENZIMIDAZOKUINAZOLIN DAN
AKTIVITI BIOLOGI MEREKA**

Oleh

HIBA ALI HASAN

April 2018

Pengerusi : Emilia binti Abd Malek, PhD
Fakulti : Sains

Diilhamkan oleh kepentingan biologi benzimidazokuinazolin, dan cubaan untuk menyelesaikan masalah rintangan bakteria dan juga ketidak seimbangan mekanisme antioksidan di dalam badan kita, dalam kajian ini, dua siri bagi lapan belas bahan terbitan dihidro- benzimidazokuinazolin (lima belas bahan terbitan baru kecuali **39**, **45**, dan **47**) telah disintesis. Dua daripada bahan terbitan ini disintesis dalam tindak balas antara 2-(2-aminofenil)-1*H*-benzimidazole dengan dua siri alifatik dan aromatik aldehid yang berlainan dalam satu langkah untuk menyiasat aktiviti-aktiviti bahan terbitan alifatik dan juga aromatik.

Sebatian-sebatian ini disintesis menggunakan dua teknik yang berbeza iaitu pemanasan tradisional menggunakan refluks dan sintesis organik berbantu-mikrogeombang. Kajian perbandingan digunakan untuk membandingkan kecekapan di antara dua protokol ini untuk mensintesis sebatian sasaran yang sama mengenai tempoh tindak balas, peratusan hasil, ketulenan sebatian, dan kebajikan terhadap alam sekitar. Tambahan pula, struktur-struktur untuk lapan belas sebatian tersebut telah disahkan dengan menggunakan TLC, analisis spektrometri (1D dan 2D NMR, FTIR, dan GCMS), analisis unsur (CHN) dan sifat fotopendarcaayaan (PL). Sewajarnya, analisis hablur tunggal telah dijalankan untuk lima sampel hablur untuk pengesahan yang lebih lanjut. Aktiviti *in vitro* anti-mikrob dan anti-kulat telah dinilai terhadap satu panel bakteria dan kulat: dua (2) Gram-positif (*Staphylococcus aureus* ATCC 43300 dan *Bacillus subtilis* UPMC 1175), dua (2) Gram-negatif (*Pseudomonas aeruginosa* ATCC 15542 dan *Salmonella choleraesuis* ATCC 10708), dan satu (1) kulat (*Aspergillus brasiliensis* ATCC 16404) untuk menguji aktiviti biologi mereka terhadap mikroorganisma yang baru. Tambahan lagi, aktiviti antioksidan ABTS dan

DPPH untuk analog-analog tersebut telah dijalankan untuk menyiasat aktiviti penipisan mereka.

Kaedah sintesis yang dipertingkatkan dengan ketuham gelombang mikro menunjukkan kelebihannya ke atas kaedah yang setandingnya untuk mensintesis jenis sebatian yang sama. Penyelidikan terhadap aktiviti antibakteria untuk kedua-dua siri sebatian (alifatik dan aromatik) menunjukkan yang beberapa sebatian memberi keupayaan yang sederhana baik untuk membantutkan pertumbuhan bakteria Gram-positif, sementara hanya satu sebatian dalam keluarga aromatik menunjukkan aktiviti pembantutan yang sangat baik berbanding dengan –tetrasiklin dadah piawai. Kedua-dua siri tidak menunjukkan apa-apa aktiviti pembantutan terhadap bakteria atau kulat Gram-negatif. Aktiviti penipisan ABTS untuk kedua-dua siri menunjukkan kecekapan yang lebih hebat daripada DPPH, dan juga beberapa analog yang lain menunjukkan aktiviti antioksidan yang sangat baik untuk kedua-dua uji kaji.

Lima belas sebatian baru bersama-sama dengan tiga analog yang diketahui disintesis untuk diuji aktiviti biologinya. Kajian mendapati bahawa dihidro-benzimidazokuinazolin disintesis dalam masa beberapa minit dengan menggunakan satu langkah sahaja untuk menghasilkan sebatian pendarfluor yang sangat tulen dengan peratusan hasil yang sangat baik (82-98%) menggunakan kaedah yang lebih mesra alam. Aktiviti-aktiviti antimikrob dan antioksidan dikaji untuk analog-analog tersebut, di mana beberapa sebatian mendedahkan aktiviti yang sangat kuat yang boleh membantu perkembangan calon ubatan pada masa hadapan.

ACKNOWLEDGEMENTS

In the name of Allah, the most gracious, the most merciful; peace and blessing for Prophet Mohammed (SAW).

First and foremost, I would like to thank my supervisor **Dr. Emilia binti Abd Malek** for her support and tremendous patience with me over the past four years. Without her understanding, encouragement, and guidance I could not continue with my study especially when I changed my project title after two years. I cannot forget her warm welcoming to her house for advice and discussion when she was on leave. This work could not brought to light without You Dr. Emilia.

My special gratitude and high appreciation goes to **Prof. Dr. Mohd Basyaruddin Abdul Rahman** and **Prof. Khozirah binti Shaari** for their co-supervision, deep comprehension, and invaluable advice through group meeting and side sessions.

A very big thanks extended to **Mr. Chan Kim Wei** (Institute of Bio Science / UPM) for his precious help in anti-oxidant evaluation. His constructive criticism broadened my knowledge and substantially assist me for preparing this thesis.

I am pleased to acknowledge **Prof. Dr. Bohari Mohd. Yamin** (Academy of Sciences Malaysia, ASM) and **Mr. Mohammed Fadzlee Ngatiman** (Center for Research and Instrumentation Management, UKM) for single crystal analysis. I get benefit from their wide knowledge in this field. Prof. Bohari was always available for discussion despite of his sickness, may Allah give him long life full with health.

I particularly indebted to thank Department of Chemistry technical staff members for their help in analyzing my samples; **Puan Shareena** and **En. Faizal** for NMR,analysis, **En. Zainal** for GCMS, **Puan Rosnani** for FTIR.

I am not forgetting the keen patience of **Cik Norihan binti Zainun Abiden** in Department of Physics for PL analysis, thank you very much.

My labmates: **Lim, Sharil, Samira, Chiya, Elmi, Piqa** and all other members of Lab 401, 105 and group meetings, I really appreciate every single moments spent together inside our lab. or outside getting lunch, celebrate Eid alfitri, or any social events spent together with our EmTech group members. Thank you Elmi for boosting my mood when I'm feeling down.

I am heartily thankful my sister **Dr. Basma M. Abd Razik** (School of Chemical Sciences/ USM; College of Pharmacy, Al-Mustansiriyah University, Baghdad, Iraq) for her continuous and truly assistance in my early research days even when she went back to Baghdad. Her input and suggestions meant a lot for me.

I gratefully appreciate **Iraqi government** to offer the opportunity and financial support to continue my study in Malaysia specifically Universiti Putra Malaysia (UPM).

Continuous prayer, unconditional love from my family especially **my parents** were the main source of power that directed and assisted me in spite of all personal hardships that I faced during my journey. Thank you mom for staying with me the whole last year taking care of me and my daughter while I am focus on my thesis. Thanks dad for being alone waiting and praying for us all that time. All these blasts of positive energy are really appreciated.

I cannot forget all the time that you spent lonely at home waiting your mom coming latte after long time in the lab. Your sweet smile and hugs make me forget all fatigues after doing my labwork, Thanks to my soul and sweetheart **Shams**.

Mere thanks to **Huda**, my elder sister, never been sufficient. She sponsor and represented me as well as work on my behalf during all the time spent here in Malaysia for PhD. pursuit. Thanks from deep of my heart to your efforts, endeavors, and being there for me.

Dhuha, and **Al-Hasan** are my little siblings. Your supplications increased my determination and give me volition to reach my goal.

My debts are many to all who has helped me during this study and not mentioned.

Thank you all,
Hiba.

I certify that a Thesis Examination Committee has met on 20 April 2018 to conduct the final examination of Hiba Ali Hasan on her thesis entitled "Microwave and Conventional Synthesis of New Dihydrobenzimidazoquinazoline Derivatives and their Biological Activities" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Doctor of Philosophy.

Members of the Thesis Examination Committee were as follows:

Mansor bin Hj. Ahmad @ Ayob, PhD

Professor
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Gwendoline Ee Cheng Lian, PhD

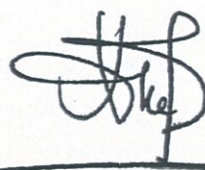
Professor
Faculty of Science
Universiti Putra Malaysia
(Internal Examiner)

Intan Safinar Ismail, PhD

Associate Professor
Faculty of Science
Universiti Putra Malaysia
(Internal Examiner)

Stephen Geoffrey Pyne, PhD

Professor
University of Wollongong
Australia
(External Examiner)



NOR AINI AB. SHUKOR, PhD

Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 28 June 2018

This thesis submitted to the Senate of Universiti Putra Malaysia has been accepted as fulfillment for the degree of Doctor of Philosophy. The members of the Supervisory committee were as follows:

Emilia Abd Malek, PhD

Senior lecturer
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Mohd Basyaruddin Abd Rahman, PhD

Professor
Faculty of Science
Universiti Putra Malaysia
(Member)

Khozirah Shaari, PhD

Professor
Faculty of Science
Universiti Putra Malaysia
(Member)

ROBIAH BINTI YUNUS, PhD

Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

Declaration by graduate student

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully-owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before thesis is published (in the form of written, printed or in electronic form) including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software.

Signature: _____ Date: _____

Name and Matric No.: Hiba Ali Hasan, GS38998

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature:
Name of
Chairman of
Supervisory
Committee:



Dr. Emilia Abd Malek

Signature:
Name of
Member of
Supervisory
Committee:



Professor Dr. Mohd Basyaruddin Abd Rahman

Signature:
Name of
Member of
Supervisory
Committee:



Professor Dr. Khozirah Shaari

TABLE OF CONTENTS

	Page
ABSTRACT	i
ABSTRAK	iii
ACKNOWLEDGEMENTS	v
APPROVAL	vii
DECLARATION	ix
LIST OF TABLES	xvi
LIST OF FIGURES	xx
LIST OF SCHEMES	xxxiii
LIST OF ABBREVIATIONS	xxxv
 CHAPTER	
1 INTRODUCTION	1
1.1 Problem Statement	3
1.2 Objectives of Study	3
 2 LITERATURE REVIEW	4
2.1 Structural and Biological Significance of Benzimidazol Compounds	4
2.2 Structural and Biological Significance of Quinazoline Compounds	5
2.3 Biological Significance of Benzimidazo[1,2-c]quinazoline	7
2.4 Synthesis of Benzimidazoquinazoline	8
2.4.1 Benzimidazoquinazolines produced from benzimidazole compounds	8
2.4.2 Benzimidazoquinazolines produced from quinazoline compounds	16
2.5 Microwave-Assisted Organic synthesis (MAOS)	19
2.5.1 Microwave Definition	19
2.5.2 Microwave Mechanisms	19
2.5.2.1 Dipolar Polarisation Mechanism	20
2.5.2.2 Conduction Mechanism	20
2.5.3 Chronological Development of Microwave-enhanced Reactions	20
2.5.4 Microwave Synthesis Instruments	21
2.5.4.1 Single-mode Microwave Instrument	21
2.5.4.2 Multi-mode Microwave Instrument	22
2.5.5 Benefits of Microwave-Assisted Synthesis	22
2.5.6 Limitations of Microwave-Assisted Technique	23
2.5.7 Microwave-Assisted Organic Synthesis (MAOS) of benzimidazoquinazoline Derivatives	23

2.6	Antioxidant Activity	28
2.6.1	Antioxidant and Free Radical Production	28
2.6.2	Antioxidant mechanisms	29
2.6.3	Antioxidant Evaluation Methods	30
2.6.4	Antioxidant Activity of benzimidazoquinazoline	31
2.7	Antimicrobial Activity	32
2.7.1	Microbial Infection and Antibiotic resistance Crisis	32
2.7.2	Antimicrobial Activity of benzimidazoquinazoline	33
2.8	Antitumor Activity	35
2.9	Other Biological Activities	36
2.10	Fluorescence study	37
2.10.1	Basic concepts in Fluorescence	37
2.10.2	Stokes Shift and the Mirror Image Rule	38
2.10.3	Absorption of Energy	40
2.10.4	Extinction Coefficient and Quantum Yield	40
2.10.5	Fluorescence Application	41
2.10.6	Fluorescence properties of benzimidazoquinazolines	41
3	MATERIALS AND METHODS	43
3.1	Materials	43
3.2	General Methods	43
3.2.1	Thin Layer Chromatography	43
3.2.2	Melting Point	43
3.2.3	Elemental Analysis	44
3.2.4	Nuclear Magnetic Resonance (NMR) Spectroscopy	44
3.2.5	Fourier Transform Infrared (FTIR) Spectroscopy	44
3.2.6	Mass Spectroscopic Analysis (MS)	44
3.2.7	Electronic Spectral Analysis	44
3.2.8	Fluorescence Emission	45
3.2.9	Optical Activity	45
3.2.10	Single Crystal Study for Structure Determination	46
3.3	Synthesis of dihydro-benzimidazoquinazoline Compounds Series [34-44]	46
3.3.1	General Method for Microwave Synthesis	46
3.3.2	General Method for Conventional Heating Synthesis	47
3.3.3	Synthesis of new 6-(<i>o</i> -tolyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>] quinazoline [34] (New)	48
3.3.4	Synthesis of new 6-(4-isopropylphenyl)-5,6-dihydrobenzo[4,5]imidazo [1,2- <i>c</i>]quinazoline [35] (New)	49
3.3.5	Synthesis of new 6-(4-(<i>tert</i> -butyl)phenyl)-5,6-dihydrobenzo[4,5] imidazo [1,2- <i>c</i>]quinazoline [36] (New)	50
3.3.6	Synthesis of new 4-(5,6-dihydrobenzo[4,5]imidazo [1,2- <i>c</i>]quinazolin-6-yl) benzonitrile [37] (New)	51
3.3.7	Synthesis of new 6-(4-phenoxyphenyl)-5,6-dihydrobenzo [4,5]imidazo [1,2- <i>c</i>] quinazoline [38] (New)	52
3.3.8	Synthesis of N-(4-(5,6-dihydrobenzo[4,5]imidazo [1,2- <i>c</i>]quinazolin-6-yl) phenyl)acetamide [39]	53

3.3.9	Synthesis of new 2-(5,6-dihydrobenzo[4,5]imidazo [1,2-c]quinazolin-6-yl)-4-methylphenol [40] (New)	54
3.3.10	Synthesis of new 2-(5,6-dihydrobenzo[4,5]imidazo [1,2-c]quinazolin-6-yl)-6-nitrophenol [41] (New)	55
3.3.11	Synthesis of new 4-(5,6-dihydrobenzo[4,5]imidazo [1,2-c]quinazolin-6-yl)-2,6-dimethoxyphenol [42] (New)	56
3.3.12	Synthesis of new 6-(4-methoxy-3-nitrophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [43] (new)	57
3.3.13	Synthesis of new 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo [1,2-c]quinazoline [44] (New)	58
3.4	Synthesis of dihydro-benzimidazoquinazolines series [45-51]	59
3.4.1	Synthesis of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo [1,2-c]quinazoline [45]	60
3.4.2	Synthesis of new 6-propyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [46] (New)	61
3.4.3	Synthesis of 6-isopropyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [47]	62
3.4.4	Synthesis of new 6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [48] (New)	63
3.4.5	Synthesis of new 6-heptyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [49] (New)	64
3.4.6	Synthesis of new 6-phenethyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [50] (New)	65
3.4.7	Synthesis of new (<i>E</i>)-6-styryl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [51] (New)	66
3.5	Antioxidant Activity	67
3.5.1	DPPH [•] Scavenging Activity	67
3.5.2	ABTS ^{•+} Scavenging Activity	67
3.5.3	Statistical Analysis	67
3.6	Antimicrobial Assay	67
3.6.1	Microbial Strain	67
3.6.2	Antimicrobial Activity	68
4	RESULTS AND DISCUSSION	69
4.1	Synthesis	69
4.1.1	Synthesis of 6-(substituted)-5,6-Dihydrobenzo[4,5]Imidazo[1,2-c]Quinazoline [34-44]	69
4.1.2	Synthesis of 6-(substituted)-5,6-Dihydrobenzo[4,5]Imidazo[1,2-c]Quinazoline [45-51].	99
4.2	Chemical Crystallography Studies	117
4.2.1	The Structure of (<i>S</i>)- <i>N</i> -(4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)phenyl)acetamide [39]	117
4.2.2	The Structure of (<i>S</i>)-2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-4-methylphenol [40]	121

4.2.3	The Structure of (<i>R/S</i>)-6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	124
4.2.4	The Structure of (<i>R/S</i>)-6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [48]	129
4.2.5	The Structure of (<i>R</i>)-6-heptyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [49]	132
4.3	Fluorescence Study	136
4.3.1	Fluorescence Study of 6-(substituted)-5,6-Dihydrobenzo [4,5] Imidazo [1,2- <i>c</i>] Quinazoline [34-44]	136
4.3.1.1	Electronic Spectral Data	136
4.3.1.2	Emission Spectral Data	138
4.3.2	Fluorescent Study of 6-(substituted)-5,6-Dihydrobenzo[4,5]Imidazo[1,2- <i>c</i>]Quinazoline [45-51]	140
4.3.2.1	Electronic Spectral Data	140
4.3.2.2	Emission Spectral data	141
4.4	Antioxidant Activity	142
4.4.1	Antioxidant Activity of 6-(substituted)-5,6-Dihydrobenzo [4,5]Imidazo [1,2- <i>c</i>]Quinazoline [34-44]	144
4.4.1.1	DPPH Scavenging Activity	144
4.4.1.2	ABTS ^{•+} Scavenging Activity	149
4.4.2	Antioxidant Activities of 6-(substituted)-5,6-Dihydrobenzo [4,5]Imidazo [1,2- <i>c</i>]Quinazoline [45-51]	153
4.4.2.1	DPPH Scavenging Activity	153
4.4.2.2	ABTS Scavenging Activity	156
4.5	Antimicrobial Study	157
4.5.1	Antimicrobial Study of 6-(substituted)-5,6-Dihydrobenzo [4,5]Imidazo [1,2- <i>c</i>]Quinazoline [34-44]	157
4.5.2	Antimicrobial Study For 6-Substituted-5,6-Dihydrobenzo [4,5]Imidazo [1,2- <i>c</i>]Quinazoline [45-51]	160
5	CONCLUSION AND RECOMMENDATIONS	163
5.1	Conclusion	163
5.2	Recommendations	164
	REFERENCES	165
	APPENDICES	177
	BIODATA OF STUDENT	280
	LIST OF PUBLICATIONS	281

LIST OF TABLES

Table	Page
4.1 Optimization reaction conditions for compound 42	69
4.2 Comparison of % yield and reaction time of benzimidazoquinazolines [34-44] between classical reflux and microwave-assisted methods	70
4.3 Physical and elemental analysis of benzimidazoquinazolines [34-44]	74
4.4 Important protons in ^1H NMR spectra of dihydro-benzimidazoquinazolines [34-44]	75
4.5 Important carbons in ^{13}C NMR spectra of dihydro-benzimidazoquinazolines [34-44]	78
4.6 ^1H - ^1H COSY, ^1H - ^{13}C HMQC, and HMBC correlations for benzimidazoquinazoline 42	82
4.7 ^1H - ^1H COSY, ^1H - ^{13}C HMQC, and HMBC correlations for benzimidazoquinazoline 44	88
4.8 FTIR frequencies of the major functional groups in dihydro-benzimidazoquinazolines [34-44]	94
4.9 The optimization reaction conditions for compound 49	100
4.10 Comparison of % yield and reaction time of dihydro-benzimidazoquinazolines [45-51] between classical reflux and microwave-assisted methods	100
4.11 Physical and elemental analysis of dihydro-benzimidazoquinazolines [45-51]	101
4.12 Important resonances in ^1H NMR spectra of dihydro-benzimidazoquinazolines [45-51]	103
4.13 Important carbons in ^{13}C NMR spectra of dihydro-benzimidazoquinazoline [45-51]	105
4.14 ^1H - ^1H COSY, ^1H - ^{13}C HMQC, and HMBC correlations for benzimidazoquinazoline 45	106
4.15 FTIR frequencies of the major functional groups in dihydro-benzimidazoquinazolines [45-51]	113

4.16	Crystal data and structure refinement for (<i>S</i>)- <i>N</i> -(4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)phenyl)acetamide [39]	118
4.17	Selected bond lengths (Å) and angles (°)	120
4.18	Hydrogen Bonds Parameters (Å) of benzimidazoquinazoline 39	121
4.19	Crystal data and structure refinement for (<i>S</i>)-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-4-methylphenol [40]	121
4.20	Selected bond lengths (Å) and angles (°)	123
4.21	Hydrogen Bonds Parameters (Å) of benzimidazoquinazoline 40	124
4.22	Crystal data and structure refinement for (<i>R/S</i>)-6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	125
4.23	Selected bond lengths (Å) and angles (°)	127
4.24	Hydrogen Bonds Parameters (Å) of benzimidazoquinazoline 44	128
4.25	Crystal data and structure refinement for (<i>R/S</i>)-6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [48]	129
4.26	Selected bond lengths (Å) and angles (°)	131
4.27	Hydrogen Bonds Parameters (Å) of benzimidazoquinazoline 48	132
4.28	Refinement of structure and crystal data for (<i>R</i>)-6-heptyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [49]	133
4.29	Selected bond lengths (Å) and angles (°)	135
4.30	Hydrogen Bonds Parameters (Å) of benzimidazoquinazoline [49]	135
4.31	Absorption and emission maxima and quantum yields (Φ) for dihydro-benzimidazoquinazolines [34-44]	139
4.32	Absorption and emission maxima and quantum yields (Φ) for dihydro-benzimidazoquinazolines [45-51]	141
4.33	DPPH [•] scavenging activities of aromatic dihydro-benzimidazoquinazolines [34-44]	145
4.34	ABTS ^{•+} scavenging activity of new synthesized aromatic series [34-44]	150
4.35	DPPH [•] scavenging activity of dihydro-benzimidazoquinazolines [45-51]	154

4.36	ABTS ^{•+} scavenging activity of dihydro-benzimidazoquinazolines [45-51]	157
4.3	Antimicrobial activities of aromatic series [34-44]	158
4.38	Antimicrobial activities of aliphatic series [45-51]	161
7.1	Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [39]. U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor	195
7.2	Bond lengths [$\text{\AA}$] and angles [$^\circ$] for [39]	196
7.3	Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [39]. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$	198
7.4	Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [39]	201
7.5	Torsion angles [$^\circ$] for [39]	202
7.6	Hydrogen bonds for [39] [$\text{\AA}$ and $^\circ$]	202
7.7	Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [40]. U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor	206
7.8	Bond lengths [$\text{\AA}$] and angles [$^\circ$] for [40]	208
7.9	Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [40]. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$	210
7.10	Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [40]	211
7.11	Torsion angles [$^\circ$] for [40]	212
7.12	Hydrogen bonds for [40] [$\text{\AA}$ and $^\circ$]	212
7.13	Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [44]. U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor	228
7.14	Bond lengths [$\text{\AA}$] and angles [$^\circ$] for [44]	230

7.15	Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [44]. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$	234
7.16	Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [44]	236
7.17	Torsion angles [$^\circ$] for [44]	237
7.18	Hydrogen bonds for [44] [$\text{\AA}$ and $^\circ$]	238
7.19	Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for compound [48]. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor	253
7.20	Bond lengths [$\text{\AA}$] and angles [$^\circ$] for [48]	254
7.21	Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [48]. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$	258
7.22	Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [48]	259
7.23	Torsion angles [$^\circ$] for [48]	260
7.24	Hydrogen bonds for [48] [$\text{\AA}$ and $^\circ$]	261
7.25	Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [49]. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor	265
7.26	Bond lengths [$\text{\AA}$] and angles [$^\circ$] for [49]	266
7.27	Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [49]. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$	268
7.28	Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for [49]	269
7.29	Torsion angles [$^\circ$] for [49]	270
7.30	Hydrogen bonds for [49] [$\text{\AA}$ and $^\circ$]	270

LIST OF FIGURES

Figure	Page
1.1 Selected clinically useful benzimidazole and quinazoline-containing drugs	2
1.2 Benzimidazoquinazoline scaffold	2
2.1 Numbering system and tautomerism in benzimidazole	4
2.2 Selected clinically available benzimidazole-containing drugs	5
2.3 Structural and general nomenclature of 2-cyano-3,4-dihydro-4-oxoquinazoline [1] and quinazoline 2	6
2.4 Selected clinically available quinazoline-containing drugs	7
2.5 Structures of benzimidazoquinazoline derivatives [3-5]	7
2.6 Ionic conduction (a) and dipole rotation (b) mechanisms. Charged particles in solution will follow the applied electric field, while dipolar molecules will try to align with an oscillating electric field	19
2.7 Single-mode microwave machine	21
2.8 Multi-mode microwave machine	22
2.9 Reaction mechanisms of antioxidant compounds with radical probe	30
2.10 Antioxidant derivatives 6-8	32
2.11 Antimicrobial compounds 9-14	33
2.12 Antimicrobial derivatives 15-18	34
2.13 Antimicrobial derivatives 19-21	34
2.14 Antifungal compound 22	35
2.15 Antitumor Compounds 23-27	36
2.16 Compounds 28-30	37
2.17 Structures of typical fluorescent substances	38
2.18 Electronic absorption and emission bands	39
2.19 Quinine absorption and emission spectra	40

2.20	Fluorescent dihydro-benzimidazoquinazolines 31-33	42
3.1	Depicted Agar Well Diffusion Technique	68
4.1	Temperature profile as effected by microwave heating (left) versus oil bath heating (right). Microwave irradiation heated the entire reaction system simultaneously, whereas in conductive heating tube, the areas in close contact with the vessel wall are heated first	71
4.2	¹ H NMR spectra of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44] with mother AMINE	77
4.3	¹³ C NMR spectra of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44] with mother AMINE	79
4.4	An expanded section for the aromatic protons in ¹ H- ¹ H COSY spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-2,6-dimethoxyphenol [42] from 6.25 to 8.0 ppm	81
4.5	Major observed correlations in ¹ H- ¹ H COSY spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	82
4.6	An expanded section for aromatic protons and carbons in ¹ H- ¹³ C HMQC NMR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-2,6-dimethoxyphenol [42]. ¹³ C NMR ranged from 102.5 to 132.5 ppm	83
4.7	An expanded section for aromatic protons and carbons in ¹ H- ¹³ C HMBC NMR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-2,6-dimethoxyphenol [42]. ¹³ C NMR ranged from 65 to 150 ppm	85
4.8	Major correlations observed between protons and carbons in ¹ H- ¹³ C HMBC spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	86
4.9	An expanded section for the aromatic protons in ¹ H- ¹ H COSY NMR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44] from 6.4 to 8.0 ppm	87
4.10	Major observed correlations in ¹ H- ¹ H COSY spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44]	88
4.11	An expanded section for aromatic protons and carbons in ¹ H- ¹³ C HMQC NMR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44]. ¹³ C NMR ranged from 107.5 to 135 ppm	89

4.12	An expanded sections of aromatic area in ^1H - ^{13}C HMBC NMR spectrum of benzimidazoquinazoline [44]. ^{13}C NMR ranged from a: 105 to 130 ppm; b: from 125 to 154 ppm	91
4.13	Major correlations observed between protons and carbons in ^1H - ^{13}C HMBC spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	92
4.14	FTIR spectrum of 2-(2-aminophenyl)-1 <i>H</i> -benzimidazole (parent primary amine)	93
4.15	FTIR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	96
4.16	Mass fragmentation spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	98
4.17	Fragmentation pattern of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	99
4.18	^1H NMR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	102
4.19	^{13}C NMR spectrum 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	104
4.20	An expanded section for the aromatic protons in ^1H - ^1H COSY NMR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45] from 6.0 to 8.0 ppm	107
4.21	Major correlations observed between protons and carbons in ^1H - ^1H COSY spectrum 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	108
4.22	An expanded section for aromatic protons and carbons in ^1H - ^{13}C HMQC NMR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]. ^{13}C NMR ranged from 110 to 130 ppm	109
4.23	An expanded section of aromatic area in ^1H - ^{13}C HMBC NMR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]. ^{13}C NMR ranged from 70 to 150 ppm	111
4.24	Major correlations observed between protons and carbons in ^1H - ^{13}C HMBC spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	112
4.25	FTIR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	114

4.26	Mass fragmentation spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	116
4.27	Fragmentation pattern of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	117
4.28	Molecular structure of (<i>S</i>)- <i>N</i> -(4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)phenyl)acetamide [39] drawn at 50% probability ellipsoid. The atoms nomenclature is specific for crystal data	119
4.29	The conformation of diazine ring of 39	119
4.30	Molecular packing of 39 viewed down <i>a</i> -axis. Non-hydrogen bonded hydrogen atoms were omitted for clarity	120
4.31	Molecular structure of (<i>S</i>)-2-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-4-methylphenol [40].drawn at 50% probability ellipsoid. The atoms nomenclature is specific for crystal data	122
4.32	The conformation of diazine ring of 40	123
4.33	Molecular packing of 40 viewed down <i>b</i> -axis. Non-hydrogen bonded hydrogen atoms were omitted for clarity	124
4.34	Molecular structure of (<i>R/S</i>)-6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44] drawn at 50% probability ellipsoid. The atoms nomenclature is specific for crystal data	126
4.35	The conformation of two diazine rings of benzimidazoquinazoline 44	127
4.36	Molecular packing of 44 viewed down <i>a</i> -axis. Non-hydrogen bonded hydrogen atoms were omitted for clarity	128
4.37	Molecular structure of (<i>R/S</i>)-6-pentyl-5,6-dihydrobenzo [4,5]imidazo [1,2- <i>c</i>]quinazoline [48] with labelling scheme drawn at 50% probability ellipsoids. The atoms nomenclature is specific for crystal data	130
4.38	The conformation of two diazine rings of 48	131
4.39	Molecular packing of benzimidazoquinazoline 48 viewed down <i>a</i> -axis. All hydrogen atoms except hydrogen bonded are omitted for clarity	132
4.40	Molecular structure of (<i>R</i>)-6-heptyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [49]. The atoms nomenclature is specific for crystal data	134
4.41	The conformation of diazine ring of 49	134

4.42	Molecular packing of benzimidazoquinazoline 49 viewed down α -axis. All hydrogen atoms except hydrogen bonded are omitted for clarity	135
4.43	UV-Vis spectrum of 2-(2-aminophenyl)-1 <i>H</i> -benzimidazole (parent primary amine)	137
4.44	UV-Vis spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-6-nitrophenol [41]	137
4.45	UV-Vis spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [49]	138
4.46	Fluorescence spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	139
4.47	UV-Vis spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	140
4.48	Fluorescence spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	142
4.49	Trolox standard curve of DPPH [•] assay	143
4.50	Trolox standard curve of ABTS ^{•+} assay	143
4.51	DPPH [•] scavenging activity for aromatic series. Means that do not share a letter are significantly different ($p < 0.05$). Error bars indicate standard error of means ($n = 3$)	145
4.52	Plausible scavenging mechanism for the reaction of DPPH radical with 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	147
4.53	ABTS ^{•+} scavenging activity for aromatic series. Means that do not share a letter are significantly different ($p < 0.05$). Error bars indicate standard error of means ($n = 3$)	150
4.54	Plausible scavenging mechanism for the reaction of ABTS radical cation with benzimidazoquinazoline 35	151
4.55	DPPH [•] scavenging activity for aliphatic series [45-51]. Means that do not share a letter are significantly different ($p < 0.05$). Error bars indicate standard error of means ($n = 3$)	153
4.56	Plausible radical scavenging mechanism for DPPH [•] reaction with 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [45]	155

4.57	ABTS ^{•+} scavenging activity for aliphatic series [45-51]. Means that do not share a letter are significantly different (p < 0.05). Error bars indicate standard error of means (n = 3)	156
4.58	Petri dishes of anti <i>Staphylococcus aureus</i> ATCC 43300 activity	159
4.59	Petri dishes of anti <i>Bacillus subtilis</i> UPMC 1175 activity	159
4.60	Petri dishes of anti <i>Staphylococcus aureus</i> ATCC 43300 activity	162
4.61	Petri dishes of anti <i>Bacillus subtilis</i> UPMC 1175 activity	162
7.1	¹ H-NMR spectrum of 6-(<i>o</i> -tolyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [34]	177
7.2	¹³ C-NMR spectrum of 6-(<i>o</i> -tolyl)-5,6-dihydrobenzo [4,5] imidazo [1,2- <i>c</i>]quinazoline [34]	177
7.3	FTIR spectrum of 6-(<i>o</i> -tolyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [34]	178
7.4	Mass spectrum of 6-(<i>o</i> -tolyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [34]	178
7.5	UV-Vis spectrum of 6-(<i>o</i> -tolyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [34]	179
7.6	Fluorescence spectrum of 6-(<i>o</i> -tolyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [34]	179
7.7	¹ H-NMR spectrum of 6-(4-isopropylphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazoline [35]	180
7.8	¹³ C-NMR spectrum of 6-(4-isopropylphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazoline [35]	180
7.9	FTIR spectrum of 6-(4-isopropylphenyl)-5,6-dihydrobenzo [4,5] imidazo[1,2- <i>c</i>]quinazoline [35]	181
7.10	GCMS fragmentation spectrum of 6-(4-isopropylphenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [35]	181
7.11	UV-Vis spectrum of 6-(4-isopropylphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazoline [35]	182
7.12	Fluorescence spectrum of 6-(4-isopropylphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazoline [35]	182
7.13	¹ H-NMR spectrum of 6-(4-(<i>tert</i> -butyl)phenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazoline [36]	183

7.14	¹³ C-NMR of 6-(4-(tert-butyl)phenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [36]	183
7.15	FTIR spectrum of 6-(4-(tert-butyl)phenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [36]	184
7.16	GCMS fragmentation spectrum of 6-(4-(tert-butyl)phenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [36]	184
7.17	UV-Vis spectrum of 6-(4-(tert-butyl)phenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [36]	185
7.18	Fluorescence spectrum of 6-(4-(tert-butyl)phenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [36]	185
7.19	¹ H-NMR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)benzonitrile [37]	186
7.20	¹³ C-NMR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)benzonitrile [37]	186
7.21	FTIR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)benzonitrile [37]	187
7.22	GCMS fragmentation spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)benzonitrile [37]	187
7.23	UV-Vis spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)benzonitrile [37]	188
7.24	Fluorescence spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)benzonitrile [37]	188
7.25	¹ H-NMR spectrum of 6-(4-phenoxyphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [38]	189
7.26	¹³ C-NMR spectrum of 6-(4-phenoxyphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [38]	189
7.27	FTIR spectrum of 6-(4-phenoxyphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [38]	190
7.28	GCMS fragmentation spectrum of 6-(4-phenoxyphenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [38]	190
7.29	UV-Vis spectrum of 6-(4-phenoxyphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [38]	191
7.30	Fluorescence spectrum of 6-(4-phenoxyphenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [38]	191

7.31	¹ H-NMR spectrum of N-(4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)phenyl)acetamide [39]	192
7.32	¹³ C-NMR spectrum of of N-(4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)phenyl)acetamide [39]	192
7.33	FTIR spectrum of of N-(4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)phenyl)acetamide [39]	193
7.34	GCMS fragmentation spectrum of of N-(4-(5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazolin-6-yl)phenyl)acetamide [39]	193
7.35	UV-Vis spectrum of of N-(4-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)phenyl)acetamide [39]	194
7.36	Fluorescence spectrum of of N-(4-(5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazolin-6-yl)phenyl)acetamide [39]	194
7.37	¹ H-NMR spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-4-methylphenol [40]	203
7.38	¹³ C-NMR spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-4-methylphenol [40]	203
7.39	FTIR spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-4-methylphenol [40]	204
7.40	GCMS fragmentation spectrum of 2-(5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazolin-6-yl)-4-methylphenol [40]	204
7.41	UV-Vis spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-4-methylphenol [40]	205
7.42	Fluorescence spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-4-methylphenol [40]	205
7.43	¹ H-NMR spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-6-nitrophenol [41]	213
7.44	¹³ C-NMR spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-6-nitrophenol [41]	213
7.45	FTIR spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-6-nitrophenol [41]	214
7.46	GCMS fragmentation spectrum of 2-(5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazolin-6-yl)-6-nitrophenol [41]	214
7.47	UV-Vis spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazolin-6-yl)-6-nitrophenol [41]	215

7.48	Fluorescence spectrum of 2-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-6-nitrophenol [41]	215
7.49	¹ H-NMR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	216
7.50	¹³ C-NMR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	216
7.51	¹ H- ¹ H COSY spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	217
7.52	¹ H- ¹³ C HMQC spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	217
7.53	¹ H- ¹³ C HMBC spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	218
7.54	FTIR spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42].	218
7.55	GCMS fragmentation spectrum of 4-(5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42].	219
7.56	UV-Vis spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	219
7.57	Fluorescence spectrum of 4-(5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-2,6-dimethoxyphenol [42]	220
7.58	¹ H-NMR spectrum of 6-(4-methoxy-3-nitrophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [43]	220
7.59	¹³ C-NMR spectrum of 6-(4-methoxy-3-nitrophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [43]	221
7.60	FTIR spectrum of 6-(4-methoxy-3-nitrophenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazoline [43]	221
7.61	GCMS fragmentation spectrum of 6-(4-methoxy-3-nitrophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [43]	222
7.62	UV-Vis spectrum of 6-(4-methoxy-3-nitrophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [43]	222
7.63	Fluorescence spectrum of 6-(4-methoxy-3-nitrophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2- <i>c</i>]quinazoline [43]	223
7.64	¹ H-NMR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2- <i>c</i>]quinazoline [44]	223

7.65	¹³ C-NMR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [44]	224
7.66	¹ H- ¹ H COSY NMR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44]	224
7.67	¹ H- ¹³ C HMQC spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44]	225
7.68	¹ H- ¹³ C HMBC NMR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44]	225
7.69	FTIR spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [44]	226
7.70	GCMS fragmentation spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [44]	226
7.71	UV-Vis spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [44]	227
7.72	Fluorescence spectrum of 6-(2,6-dichlorophenyl)-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [44]	227
7.73	¹ H-NMR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [45]	239
7.74	¹³ C-NMR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [45]	239
7.75	¹ H- ¹ H COSY NMR spectrum of 6-ethyl-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [45]	240
7.76	¹ H- ¹³ C HMQC spectrum of 6-ethyl-5,6-dihydrobenzo [4,5]imidazo [1,2-c]quinazoline [45]	240
7.77	¹ H- ¹³ C HMBC spectrum of 6-ethyl-5,6-dihydrobenzo [4,5]imidazo[1,2-c] quinazoline [45]	241
7.78	FTIR spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [45]	241
7.79	GCMS fragmentation spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [45]	242
7.80	UV-Vis spectrum of 6-ethyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [45]	242
7.81	Fluorescence spectrum of 6-ethyl-5,6-dihydrobenzo[4,5] imidazo[1,2-c]quinazoline [45]	243

7.82	¹ H-NMR spectrum of 6-propyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [46]	243
7.83	¹³ C-NMR spectrum of 6-propyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [46]	244
7.84	FTIR spectrum of 6-propyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [46]	244
7.85	GCMS fragmentation spectrum of 6-propyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [46]	245
7.86	UV-Vis spectrum of 6-propyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [46]	245
7.87	Fluorescence spectrum of 6-propyl-5,6-dihydrobenzo[4,5]imidazo[1,c]quinazoline [46]	246
7.88	¹ H-NMR spectrum of 6-isopropyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [47]	246
7.89	¹³ C-NMR spectrum of 6-isopropyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [47]	247
7.90	FTIR spectrum of 6-isopropyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [47]	247
7.91	GCMS fragmentation spectrum of 6-isopropyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [47]	248
7.92	UV-Vis spectrum of 6-isopropyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [47]	248
7.93	Fluorescence spectrum of 6-isopropyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [47]	249
7.94	¹ H-NMR spectrum of 6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [48]	249
7.95	¹³ C-NMR spectrum of 6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [48]	250
7.96	FTIR spectrum of 6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [48]	250
7.97	GCMS fragmentation spectrum of 6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [48]	251
7.98	UV-Vis spectrum of 6-pentyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [48]	251

7.99	Fluorescence spectrum of 6-pentyl-5,6-dihydrobenzo[4,5] imidazo [1,2-c]quinazoline [48]	252
7.100	¹ H-NMR spectrum of 6-heptyl-5,6-dihydrobenzo[4,5] imidazo [1,2-c]quinazoline [49]	262
7.101	¹³ C-NMR spectrum of 6-heptyl-5,6-dihydrobenzo[4,5] imidazo [1,2-c]quinazoline [49]	262
7.102	FTIR spectrum of 6-heptyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c] quinazoline [49]	263
7.103	GCMS fragmentation spectrum of 6-heptyl-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [49]	263
7.104	V-Vis spectrum of 6-heptyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c] quinazoline [49]	264
7.105	Fluorescence spectrum of 6-heptyl-5,6-dihydrobenzo [4,5]imidazo [1,2-c]quinazoline [49]	264
7.106	¹ H-NMR spectrum of 6-phenethyl-5,6-dihydrobenzo [4,5] imidazo [1,2-c]quinazoline [50]	271
7.107	¹³ C-NMR of 6-phenethyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c] quinazoline [50]	271
7.108	FTIR spectrum of 6-phenethyl-5,6-dihydrobenzo[4,5] imidazo[1,2- c]quinazoline [50]	272
7.109	GCMS fragmentation spectrum of 6-phenethyl-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [50]	272
7.110	UV-Vis spectrum of 6-phenethyl-5,6-dihydrobenzo[4,5] imidazo [1,2-c]quinazoline [50]	273
7.111	Fluorescence spectrum of 6-phenethyl-5,6-dihydrobenzo[4,5] imidazo[1,2-c]quinazoline [50]	273
7.112	¹ H-NMR spectrum of (E)-6-styryl-5,6-dihydrobenzo[4,5] imidazo[1,2-c]quinazoline [51]	274
7.113	¹³ C-NMR spectrum of (E)-6-styryl-5,6-dihydrobenzo[4,5] imidazo[1,2-c]quinazoline [51]	274
7.114	FTIR spectrum of (E)-6-styryl-5,6-dihydrobenzo[4,5] imidazo [1,2-c]quinazoline [51]	275
7.115	GCMS fragmentation spectrum of (E)-6-styryl-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [51]	275

7.116	UV-Vis of (E)-6-styryl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline [51]	276
7.117	Fluorescence spectrum of (E)-6-styryl-5,6-dihydrobenzo [4,5]imidazo[1,2-c]quinazoline [51]	276
7.118	Images of benzimidazoquinazolines 29-36	277
7.119	Images of benzimidazoquinazolines 37-44	278
7.120	Images of benzimidazoquinazolines 45 and 46	279



LIST OF SCHEMES

Scheme		Page
2.1	Base-catalyzed synthesis of benzo[4,5]imidazo[1,2- <i>a</i>]quinazoline	8
2.2	Synthesis of benzimidazo[1,2- <i>a</i>]quinazolines catalyzed by CuI/L-proline	9
2.3	[H ₂ -DABCO][H ₂ SO ₄] ₂ -catalysed synthesis of benzimidazoquinazolinones	10
2.4	Ultrasonic synthesis of benzimidazo[2,1- <i>b</i>]quinazolin-1 (1H)-ones	11
2.5	Chitosan-supported ferrite nanocomposite-catalyzed synthesis of benzimidazo[2,3- <i>b</i>]quinazolinones	12
2.6	Synthesis of substitutedbenzimidazo[1,2- <i>c</i>][1,2,4]triazolo[4,3- <i>a</i>]quinazolines	12
2.7	Synthesis of benzimidazo[1,2- <i>a</i>]pyrazolo-[1,5- <i>c</i>]quinazoline	13
2.8	Aza-Wittig reaction of iminophosphorane with heterocumulenes to synthesis benzimidazo[1,2- <i>c</i>]quinazolines	14
2.9	Synthesis of (substituted-benzo[4,5]imidazo[1,2- <i>c</i>]quinazolin-6-yl)-allyl-amine	15
2.10	Copper-catalyzed cascade synthesis of benzimidazoquinazoline derivatives	15
2.11	Synthesis of 5,6-dihydro-6-aryldiene-benzimidazo[1,2- <i>c</i>]quinazolines and 6-substituted benzimidazo[1,2- <i>c</i>]quinazolines	16
2.12	CuI-catalyzed synthesis of benzimidazo[1,2- <i>c</i>]quinazolines	17
2.13	Synthesis of S-alkyl derivatives of benzimidazo[1,2- <i>c</i>]quinazolines	18
2.14	Metal free C-N couplings synthesis of benzimidazo[1,2- <i>c</i>]quinazolines	18
2.15	Synthesis of benzimidazo[1,2- <i>a</i>]quinazolines using metal-free microwave-assisted conditions	24
2.16	Microwave synthesis of benzimidazoquinazolines	24

2.17	Microwave synthesis of indolo[1,2- <i>c</i>]quinazolines and benzimidazo[1,2- <i>c</i>]quinazolines	25
2.18	Microwave assisted synthesis of 12-arylbenzimidazo[2, 1- <i>b</i>]quinazolin-1(2H)-ones	26
2.19	Microwave synthesis of 6-arylbenzimidazo[1,2- <i>c</i>]quinazolines	27
2.20	Synthesis of benzimidazoquinazolinones: (A) Microwave assisted solid-phase synthesis and (B) Microwave assisted solution-phase synthesis	28
3.1	General synthesis scheme for dihydro-benzimidazoquinazolines [34-44]	47
3.2	General scheme for synthesis quinazolines [45-51]	59
4.1	Plausible mechanism for dihydro-benzimidazoquinazoline formation	73

LIST OF ABBREVIATIONS

Å	Angstrom
δ	Chemical shift
CHN	Carbon, Hydrogen, and Nitrogen
DIMS	Direct Injection Mass Spectroscopy
DMF	Dimethylformamide
DMSO	Dimethyl Sulfoxide
eV	Electron Volt
FTIR	Fourier Transform Infrared
GCMS	Gas Chromatography Mass Spectroscopy
GHz	Giga Hertz
Hz	Hertz
IC ₅₀	Half Inhibitory Concentration
<i>J</i>	NMR Coupling Constant
M	Molar concentration
MHz	Mega Hertz
MIC	Minimum Inhibitory Concentration
mp	Melting Point
MS	Mass Spectroscopy
MW	Microwave
<i>m/z</i>	Mass to Charge ratio
NMP	N-methyl-2-pyrrolidone
SD	Standard Deviation
R _f	Retention factor
RSD	Relative Standard Deviation
THF	Tetrahydrofuran
TLC	Thin layer Chromatography
NMR	Nuclear Magnetic Resonance
Uv-Vis	Ultraviolet Visible

CHAPTER 1

INTRODUCTION

Heterocyclic compounds occupy a central position in medicinal and organic chemistry, with considerable attention concentrating on their syntheses. Nitrogen-containing heterocycles are ubiquitous backbones found in natural products, medicine and organic materials. They exhibit diverse biological and pharmacological activities partially due to their similarities to many natural and synthetic molecules with known biological activities (Pang *et al.*, 2015; Rohini *et al.*, 2010). Fused-ring heterocyclic compounds containing nitrogen are frequently studied owing to their diverse biological and pharmaceutical properties. Indeed, designing novel heterocyclic motifs has rapidly become an increasingly urgent mission for chemists. (Chen *et al.*, 2016).

Quinazoline derivatives, which belong to the N-containing heterocyclic compounds, have likewise caused universal interest due to their broad and distinct biopharmaceutical activities. Researchers have already determined many therapeutic activities of quinazoline derivatives, including anti-cancer, anti-inflammation, anti-bacterial, analgesia, anti-viral, anticytotoxin, anti-spasm, anti-tuberculosis, anti-oxidant, antimalarial, anti-hypertension, anti-obesity, anti-psychosis, and anti-diabetic, etc., (Shen *et al.*, 2016; Zayed and Hassan, 2014; Asif, 2014; Wang and Gao, 2013; Desai *et al.*, 2013; Kaur *et al.*, 2011; Aly *et al.*, 2010).

Accordingly, medicinal chemists have synthesised a variety of quinazoline compounds with different biological activities by introducing various active groups to the quinazoline moiety using progressive synthetic methods. The potential applications of the quinazoline derivatives in the fields of biology, pesticides and medicine have also been investigated (Wang and Gao, 2013).

In turn, benzimidazole derivatives are important nitrogen-comprising heterocycles which constitute useful intermediates in organic synthesis, and over the past few years, there has been a growing interest towards the examination of these compounds as it can be considered an interesting tool for the development of compounds exerting biological properties (Davoodnia *et al.*, 2007; Via *et al.*, 2001). Benzimidazole containing compounds display a broad range of therapeutic activities, including antimicrobial, antitumor, and antibacterial activities and are also used as inhibitors of PI3-kinase α and the potent antistaphylococcal agents with dual inhibitory mechanisms against DNA gyrase (Li *et al.*, 2014; Gurvinder *et al.*, 2013; Singh *et al.*, 2012). Many clinically used drugs contain quinazoline and benzimidazole moieties. **Figure 1.1** displays those important clinical drugs (Mahire *et al.*, 2016; Li, *et al.*, 2014; Saha *et al.*, 2007).

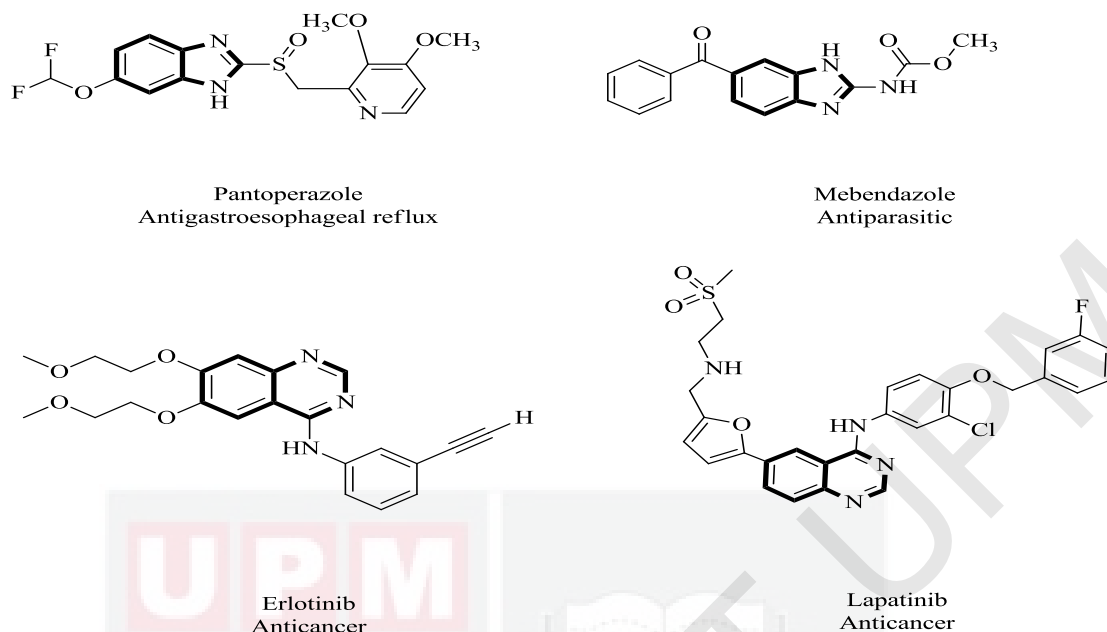


Figure 1.1 : Selected clinically useful benzimidazole and quinazoline-containing drugs.

Given the several interesting properties of these two moieties, it is postulated that introduction of benzimidazole group into the quinazoline system would be a useful strategy for designing a new class of drugs which appreciably, will influence the biological activity. Notwithstanding, many previous literature reported the pharmaceutical properties of quinazoline-fused benzimidazole skeleton. **Figure 1.2** illustrates the attractive fused scaffold consisting of both benzimidazole and quinazoline.

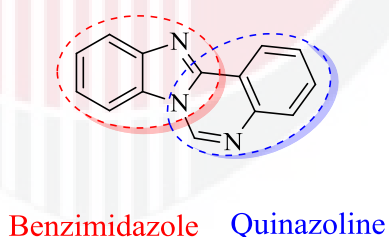


Figure 1.2 : Benzimidazoquinazoline scaffold.

Review of the previous literature that studied benzimidazoquinazolines has also revealed that those derivatives are fluorescent and emit light under ultraviolet source. The benzimidazoquinazoline derivatives were used as chemo-sensor and fluorescent probe for sequential recognition (Tang *et al*, 2013; Jeyanthi *et al*, 2013).

Recently, microwave-assisted reactions have attracted significant research interest because of the simplicity of operation and enhanced reaction rates (Davoodnia, 2010). Indeed, motivated by these results, along with interest in the utilisation of microwave irradiation for the synthesis of heterocyclic compounds, a rapid and efficient synthesis of some dihydro-benzimidazo[1,2-*c*]quinazolines through cyclocondensation of 2-(1H-benzimidazol-2-yl) aniline and different series of aldehydes with a catalytic amount of acetic acid under microwave irradiation is hence, investigated and reported in this study.

1.1 Problem Statement

There are innate defense mechanisms in human bodies to scavenge free radicals (generated in the body as a result of redox reactions) in order to sustain the homeostasis. However, the imbalance of such mechanisms leads to the progression of oxidative stress and numerous diseases, especially various chronic and age-related ones such as carcinogenesis, inflammation, and atherogenesis. As important supplements to the scavenging mechanisms, antioxidants (both naturally occurring and synthetic) have been widely applied in pharmaceuticals, foods, and cosmetics (Zhang *et al.*, 2014). In addition, good antioxidant compounds are good potential leads for further physiological and biological activities. Therefore there is growing request to design and synthesise new antioxidants for pharmaceutical use.

On the other hand, the bacterial resistance to the available antibiotics have reached to the level of crisis. That has attributed to the overuse and misuse of these medications, as well as a lack of new drug development by the pharmaceutical industry due to reduced economic incentives and challenging regulatory requirements. This has led to fears of a “postantibiotic era” in which many bacterial infections will be untreatable (Ventola, 2015). Despite the large number of antibiotics available for medical use, design and synthesis of new potent antimicrobial agents is still in demand because of acquired resistance against old and new antibiotics.

1.2 Objectives of Study

This work aims to synthesise a library of new dihydro-benzimidazoquinazoline compounds with good biological activity that could be further possibly developed as drug candidates. The specific objectives were set as the following:

To synthesise two series dihydro-benzimidazoquinazoline derivatives using microwave and conventional methods.

To characterize the physicochemical properties of the synthesised compounds.

To investigate their antioxidant and antimicrobial activities.

REFERENCES

- Adam, F., Arafath, M. A., Rosenani, A. H., and Razali, M. R. (2015). Crystal structure of 5-(5,6-dihydro- benzo[4,5]imidazo[1,2-c]quinazolin-6- yl)-2-methoxyphenol. *Acta Crys. Sect E*, *E71*, 0971–0972.
- Alam, M. N., Bristi, N. J., and Rafiquzzaman, M. (2013). Review on in vivo and in vitro methods evaluation of antioxidant activity. *Saudi Pharmaceutical Journal*, *21*(2), 143–152.
- Aly, A. A. (2007). Synthesis and Antimicrobial Activity of Some Annelated Quinazoline Derivatives. *Journal of the Chinese Chemical Society*, *54*, 437–446.
- Aly, M. M., Mohamed, Y. A., El-Bayouki, K. A. M., Basyouni, W. M., and Abbas, S. Y. (2010). Synthesis of some new 4 (3 H) -quinazolinone-2-carboxaldehyde thiosemicarbazones and their metal complexes and a study on their anticonvulsant , analgesic , cytotoxic and antimicrobial activities e Part-1. *Europian Journal of Medicinal Chemistry*, *45*, 3365–3373.
- Anitha, C., Sheela, C. D., Tharmaraj, P., and Shanmugakala, R. (2013). Studies on Synthesis and Spectral Characterization of Some Transition Metal Complexes of Azo-Azomethine Derivative of Diaminomaleonitrile. *International Journal of Inorganic Chemistry*, 1–10.
- Asif, M. (2014). Chemical Characteristics , Synthetic Methods , and Biological Potential of Quinazoline and Quinazolinone Derivatives. *International Journal of Medicinal Chemistry*, 1–27.
- Bahekar, R. H., and Rao, A. R. R. (2000). Bronchodilation and Structure-Activity Relationship Studies on New 6-Substituted Benzimidazo [1 , 2-c] quinazolines. *Arzneim.-Forsch./Drug Res.*, *50 (II)*(8), 712–716.
- Bandgar, B. P., Gawande, S. S., Bodade, R. G., Totre, J. V., and Khobragade, C. N. (2010). Synthesis and biological evaluation of simple methoxylated chalcones as anticancer , anti-inflammatory and antioxidant agents. *Bioorganic & Medicinal Chemistry*, *18*, 1364–1370. doi:10.1016/j.bmc.2009.11.066
- Bansal, Y., and Silakari, O. (2012). The therapeutic journey of benzimidazoles : A review. *Bioorganic & Medicinal Chemistry*, *20*, 6208–6236.
- Bayoumi, W. A., Barghash, A. M., Gineinah, M. M., Mohamed, A., & Abdelal, A. M. (2014). Design , synthesis and antioxidant evaluation of certain new phthalazine derivatives. *Der Pharma Chemica*, *6*(3), 89–102.
- Bennett, L. L., Rojas, S., and Seefeldt, T. (2015). Role of Antioxidants in the Prevention of Cancer. *Journal of Experimental and Clinical Medicine*, *4*(4), 215–222.

- Boligon, A. A., Machado, M. M., and Athayde, M. L. (2014). Technical Evaluation of Antioxidant Activity. *Medicinal Chemistry*, 4(7), 517–522.
- Brana, M. F., de Vaga, M. J. P., Perron, D., Colon, D., Bousquet, P. F., and Robinson, S. P. (1997). Benzimidazo[1,2-c]quinazoline Dimers as Potential Antitumor Agents. *J.Heterocyclic Chem*, 34, 807–812.
- British Pharmacopeia. (2013). (17th ed.). The Stationary office on behalf of the Medicines and Healthcare Products Regulatory Agency (MHRA).
- Bubbly, S. G., Gudennavar, S. B., Gowda, N. M. N., Bhattacharjee, R., and Natarajan, V. G. S. (2012). Synthesis, Characterization and Biological Activity Studies on 6-p-Dimethylaminophenyl-5,6-dihydrobenzoimidazo[1,2-c]quinazoline: Crystal Structure of the Title Compound and Comparative Study with Related Derivatives. *Journal of Chemical Crystallography*, 42, 305–312.
- Carpenter, R. D., Lam, K. S., and Kurth, M. J. (2007). Microwave-Mediated Heterocyclization to Benzimidazo [2 , 1- b] quinazolin-12 (5 H) -ones. *J. Org. Chem.*, 72(1), 284–287.
- Cerretani, L., and Bendini, A. (2010). *Rapid Assays to Evaluate the Antioxidant Capacity of Phenols in Virgin Olive Oil. Olives and Olive Oil in Health and Disease Prevention*. Elsevier Inc.
- Chan, K. W., Khong, N. M. H., Iqbal, S., Mansor, S. M., and Ismail, M. (2013a). Defatted kenaf seed meal (DKSM): Prospective edible flour from agricultural waste with high antioxidant activity. *LWT - Food Science and Technology*, 53(1), 308–313.
- Chan, K.W., Khong, N. M. H., Iqbal, S., and Ismail, M. (2013b). Isolation and antioxidative properties of phenolics-saponins rich fraction from defatted rice bran. *Journal of Cereal Science*, 57, 480–485.
- Chen, L.H., Chung, Tw., Narhe, B. D., and Sun, C. (2016). A Novel Mechanistic Study on Ultrasound-Assisted, One-Pot Synthesis of Functionalized Benzimidazo[2,1 - b]quinazolin-1(1 H) - ones. *ACS Combinatorial Science*, 18, 162–169.
- Dallinger, D., and Kappe, C. O. (2007). Microwave-Assisted Synthesis in Water as Solvent. *Chemical Reviews*, 107(6), 2563–2591.
- Davoodnia, A. (2010). Microwave Assisted Synthesis of Fused Benzimidazoles. *Asian Journal of Chemistry*, 22(2), 1591–1594.
- Davoodnia, A., Heravi, M. M., Golshani, E., Bakavoli, M., and Dehabadi, L. (2007). Synthesis of novel benzimidazo[1,2-c][1,2,4]triazolo[4,3-a]quinazoline derivatives. *Journal of Chemical Research*, may, 257–258.

- Dawidowicz, A. L., Olszowy, M. (2013). The importance of solvent type in estimating antioxidant properties of phenolic compounds by ABTS assay. *Eur Food Res Technol*, 236, 1099–1105.
- Desai, N. C., Dodiya, A., and Shihory, N. (2013). Synthesis and antimicrobial activity of novel quinazolinone – thiazolidine – quinoline compounds. *Journal of Saudi Chemical Society*, 17, 259–267.
- Elansary, H. O. (2014). Plant Biochemistry & Physiology Natural Antioxidants and their Role against Human Cancer. *Plant Biochemistry & Physiology*, 2(2), 1–2.
- Eltayeb, N. E., Teoh, S. G., and Lo, K. M. (2011). supporting information. *Acta Cryst. Sect E*, E67, 02519.
- Fang, S., Niu, X., Yang, B. Li, Y., & Si, X., Feng, L., and Ma, C. (2014). One-pot Synthesis of Benzo [4 , 5] imidazo [1 , 2- a] quinazoline Derivatives via Facile Transition Metal-free Tandem Process. *ACS Combinatorial Science*, 1–17.
- Foo, C. F., Yusoff, F. M., Ismail, M., Basri, M., Chan, K. W., Khong, N. M. H., and Yau, S. K. (2015). Production of fucoxanthin-rich fraction (FxRF) from a diatom , *Chaetoceros calcitrans* (Paulsen) Takano 1968. *Algal Research*, 12, 26–32.
- Foo, S. C., Yusoff, F. M., Ismail, M., Basri, M., Khong, N. M. H., Chan, K. W., and Yau, S. K. (2015). Efficient solvent extraction of antioxidant-rich extract from a tropical diatom, *Chaetoceros calcitrans* (Paulsen) Takano 1968. *Asian Pacific Journal of Tropical Biomedicine*, 5(10), 834–840.
- Fre `re, S., Thie ´ry, V., Bailly, C., and Besson, T. (2003). Novel 6-substituted benzothiazol-2-yl indolo[1,2-c]quinazolines and benzimidazo[1,2-c]quinazolines. *Tetrahedron*, 59, 773–779.
- Gaba, M., and Dhingra, N. (2011). Microwave Chemistry : General Features and Applications. *Indian Journal of Pharmaceutical Education and Research*, 45(2), 175–183.
- Gaba, M., Singh, S., and Mohan, C. (2014). Benzimidazole : An emerging scaffold for analgesic and anti-in fl ammatory agents. *European Journal of Medicinal Chemistry*, 76, 494–505.
- Galarce, G. D., Foncea, R. E., Edwards, A. M., Pessoa-Mahana, H., Pessoa-Mahana C. D., and Ebensperger, R. A. (2008). Biological evaluation of novel 6-Arylbenzimidazo [1,2-c] quinazoline derivatives as inhibitors of LPS-induced TNF- alpha secretion. *Biologocal Reseaech*, 41, 1–7.
- Gawande, M. B., Shelke, S. N., Zboril, R., and Varma, R. S. (2014). Microwave-Assisted Chemistry : Synthetic Applications for Rapid Assembly of Nanomaterials and Organics. *Accounts of Chemical Research*, 47, 1338–1348.

- Glasnov, T. N., and Kappe, C. O. (2007). Microwave-Assisted Synthesis under Continuous-Flow Conditions. *Macromol. Rapid Commun.*, 28, 395–410.
- Grewal, A. S., Kumar, K., Redhu, S., and Bhardwaj, S. (2013). Microwave assisted synthesis : a green chemistry approach. *Int. Res J Pharm. App Sci.*, 3(5), 278–285.
- Gurvinder, S., Maninderjit, K., & Mohan, C. (2013). Benzimidazoles: The Latest Information on Biological Activities. *International Research Journal of Pharmacy*, 4(1), 82–87.
- Hasan, H. A., A., MR. Raauf, Razik, B. M. AR., and Hassan, B. A. (2012). Chemical Composition-and-Antimicrobial Activity of the Crude Extracts Isolated from Zingiber Officinale by Different Solvents. *Pharmaceutica Analytica Acta*, 3(9), 1–5.
- Hauser, A. R., Mecsas, J., & Moir, D. T. (2016). Beyond Antibiotics : New Therapeutic Approaches for Bacterial Infections. *Healthcare Epidemiology*, 63(1 July), 89–95.
- Herman, B., Frohlich, V. E. C., Lakowicz, J. R., Murphy, D. B., Spring, K. R., and Davidson, M. W. (2017). Basic Concepts in Fluorescence. <https://micro.magnet.fsu.edu/primer/techniques/fluorescence/fluorescenceintro.html>
- Hussein, M. A. (2013). Synthesis, anti-inflammatory, and structure antioxidant activity relationship of novel 4-quinazoline. *Medicinal Chemistry Research*, 22, 4641–4653.
- Ilangovan, A., Anandhan, K., Prasad, K. M., Vijayakumar, P., Renganathan, R., Ananth, D. A., & Sivasudha, T. (2014). Synthesis , DNA-binding study , and antioxidant activity of 14-aryl-14 H -dibenzo [a , j] xanthene derivatives. *Med Chem Res*, 1–12.
- Insuasty, B. A., Torres, H., Quiroga, J., Abonia, R., Rodriguez, R., Nogeras, M., Sanchez, A., Saitz, C., Alvarez, S. L., and Zacchino, S. A. (2006). Synthesis, characterization and in vitro antifungal evaluation of novel benzimidazo[1,2-c]quinazolines. *Journal of the Chilean Chemical Society*, 51(2), 927–932.
- Ivachtchenko, A., Kovalenko, S., and Drushlyak, O. (2002). Synthesis of Benzimidazo[1,2-c]quinazoline-6(5H)-thiones. *Heterocyclic Communications*, 8(3), 233–236.
- Jakovljević , K., Matic´ , I. Z., Stanojković , T., Krivokuc´ a , A., Marković , V., Joksović , M. D., Mihailović , N., Nic´ iforović , M., and Joksović, L. (2017). Synthesis , antioxidant and antiproliferative activities of 1 , 3 , 4-thiadiazoles derived from phenolic acids. *Bioorganic & Medicinal Chemistry Letters*, 27, 3709–3715.

- Jeyanthi, D., Iniya, M., Krishnaveni, K., and Chellappa, D. (2013). A ratiometric fluorescent sensor for selective recognition of Al^{3+} ions based on a simple benzimidazole platform. *RSC Advances*, 1–6.
- Jia, H., Pu, S., Fan, C., Liu, G., and Zheng, C. (2015). A highly selective ratiometric fluorescent Cu^{2+} and HSO_4^- probe based on a new photochromic diarylethene with a 6-aryl[1,2-c]quinazoline unit. *Dyes and Pigments*, 121, 211–220.
- Jiang, XF., XL., Ye, Zhang, B., Li, XG., and Liu, X. (2011). Synthesis and Antimicrobial Activity of 8-Alkyl Coptisine Derivatives. *Asian Journal of Chemistry*, 23(9), 3849–3852.
- Joshi, P. P., and Shirodkar, S. G. (2014). A new approach for the synthesis of 6-aryl-5,6-dihydrobenzimidazo[1,2-c]quinazoline derivatives and its biological study. *World Journal of Pharmacy and Pharmaceutical Sciences*, 3(9), 950–958.
- Kappe, C. O. (2002). High-speed combinatorial synthesis utilizing microwave irradiation. *Current Opinion in Chemical Biology*, 6, 314–320.
- Kappe, C. O. (2004). Controlled Microwave Heating in Modern Organic Synthesis. *Angew. Chem. Int. Ed.*, 43, 6250–6284.
- Kappe, C. O. (2008). Microwave dielectric heating in synthetic organic chemistry. *Chemical Society Reviews*, 37, 1127–1139.
- Kappe, C. O., Pieber, B., and Dallinger, D. (2013). Microwave Effects in Organic Synthesis : Myth or Reality ? *Angew. Chem. Int. Ed.*, 52, 1088–1094.
- Kapoor, P., Fahmi, N., and Singh, R. V. (2011). Microwave assisted synthesis, spectroscopic, electrochemical and DNA cleavage studies of lanthanide(III) complexes with coumarin based imines. *Spectrochimica Acta Part A*, 83, 74–81.
- Kaur, R., Bansal, M., and Kaur, B. (2011). Synthesis of Some New Quinazoline Derivatives and Theoretical Studies of their Geometries. *Chemical Sciences Journal*, (CSJ-18), 1–9.
- Kedare, S. B., and Singh, R. P. (2011). Genesis and development of DPPH method of antioxidant assay. *J Food Sci Technol*, 48(4), 412–422.
- Kemegne, G. A., Mkounga, P., J. J. E., Ngang, S. L. S., Kamdem, and A. E., N. (2017). Antimicrobial structure activity relationship of five anthraquinones of emodine type isolated from *Vismia laurentii*. *BMC Microbiology*, 17(41), 1–8.
- Keri, R. S., Hiremathad, A., Budagumpi, S., and Nagaraja, B. M. (2015). Comprehensive Review in Current Developments of Benzimidazole - Based Medicinal Chemistry. *Chem Biol Drug Des*, 86(1), 19–65.
- Kidwai, M., Saxena, S., Khan, M. K. R., and Thukral, S. S. (2005). Synthesis of 4-aryl-7,7-dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2-one/thione-5-one

derivatives and evaluation as antibacterials. *European Journal of Medicinal Chemistry*, 40, 816–819.

Kuarm, B. S., Reddy, Y. T., Madhav, J. V., Crooks, P. A., and Rajitha, B. (2011). 3-[Benzimidazo- and 3-[benzothiadiazoleimidazo-(1,2-c)quinazolin-5-yl] -2H-chromene-2-ones as potent antimicrobial agents. *Bioorganic & Medicinal Chemistry Letters*, 21, 524–527.

Kumar, B. D., and Rawat, D. S. (2013). Synthesis and antioxidant activity of thymol and carvacrol based Schiff bases. *Bioorganic & Medicinal Chemistry Letters*, 23, 641–645.

Kumar, P., Singh, A. K., Bahadur, V., Len, C., Richards, N. G. J., Parmar, V. S., Eycken, E. V. V. E., and Singh, B. K. (2016). Microwave Assisted Metal Free , Base mediated C-N Bond Formation / Cleavage : Synthesis of Benzimidazo [1 , 2- a] quinazoline Derivatives. *Sustainable Chemistry & Engineering*, 1–16.

Lahsasni, S. A., Al Korbi, F., H., and Aljaber, N. A. (2014). Synthesis , characterization and evaluation of antioxidant activities of some novel chalcones analogues. *Chemistry Central Journal*, 8(32), 1–10.

Lakowicz, J. R. (2008). *Principles of Fluorescence Spectroscopy* (Third edit.). Springer.

Lamazzi, C., Leonce, S., Pfeiffer, B., Renard, P., Guillaumet, G., Rees, C. W., and B. T. (2000). Expeditious Synthesis and Cytotoxic Activity of New Cyanoindolo [3 , 2- c] quinolines and Benzimidazo [1 , 2- c] quinazolines. *Bioorganic & Medicinal Chemistry Letters*, 10, 2183–2185.

Li, C., Zhang, WT., and Wang, X. (2014). CuI-Catalyzed C – N Bond Formation and Cleavage for the Synthesis of Benzimidazo[1,2 - a]quinazoline Derivatives. *The Journal of Organic Chemistry*, A–E.

Li, Z. C., Kong, X. B., Mai, W. P., Sun, G. C. and Zhao, S. Z. (2015). Synthesis and Antimicrobial Activity of 9-O-Substituted Palmatine Derivatives. *Indian J Pharm Sci*, 77(2), 196–201.

Liang, N. and, & Kitts, D. D. (2014). Antioxidant Property of Coffee Components: Assessment of Methods that Define Mechanisms of Action. *Molecules*, 19, 19180–19208.

Lidstrom, P., Tierney, J., Wathey, B., and Westman, J. (2001). Microwave assisted organic synthesis-a review. *Tetrahedron*, 57, 9225–9283.

Lin, Z. (2010). *Novel Microwave-Mediated Luminescent Chromophore Synthesis for Photophysical Study*.

Lipunova, G. N., Mokrushina, G. A., Granovskaya, E. B., Chasovskikh, O. M., Charushin, V. N. (1996). Benzimidazo [1 , 2- a] pyrazolo [1 , 5- c] quinazoline :

- a novel heterocyclic system. *Mendeleev Communications*, 6(1), 15–17.
- Los, R., Wesołowska-trojanowska, M., Malm, A., Karpinska, M. M., Matysiak, J., Niewiadomy, A., & Głaszcz, U. (2012). A New Approach to the Synthesis of Quinazolines , and Other Related Compounds and Their Antibacterial Activity. *Heteroatom Chemistry*, 23(3), 265–275.
- Maddila, S., Gorle, S., Seshadri, N., Lavanya, P., and Jonnalagadda, S. B. (2016). Synthesis , antibacterial and antifungal activity of novel benzothiazole pyrimidine derivatives. *Arabian Journal of Chemistry*, 9, 681–687.
- Mahire, V. N., Patel, V. E., and Mahulikar, P. P. (2016). Facile DES-mediated synthesis and antioxidant potency of benzimidazoquinazolinone motifs. *Research on Chemical Intermediates*, 1–15.
- Maleki, A., and Ghamari, N. (2013). A three-component one-pot procedure for the synthesis benzimidazolo- quinazolinone derivatives in the presence of chitosan-supported metal nanocomposite as a green and reusable catalyst. *ECSOC*, 1–9.
- McMurry, J. (2008). Structure Determination: Mass Spectrometry and Infrared Spectroscopy. In *Organic chemistry* (Seventh Ed., p. 409). Belmont, CA: Thomson Brooks/cole.
- Mehta, S., Swarnkar, N., Vyas, M., Vardia, J., Punjabi, P. B., and Ameta, S. C. (2007). Synthesis and Characterization of Some Quinazoline Derivatives as Potential Antimicrobial Agents under Microwave Irradiation. *Bull. Korean Chem. Soc.*, 28(12), 2338–2342.
- Miliovsky, M., Svinyarov, I. Prokopova, E., Batovska, D., Stoyanov, S., Bogdanov, M. G. (2015). Synthesis and Antioxidant Activity of Polyhydroxylated trans-Restricted 2-Arylcinnamic Acids. *Molecules*, 20, 2555–2575.
- Molina, P., Alajarin, M., and V. A. (1989). New methodology for the preparation of quinazoline derivatives via tandem aza-Wittig/heterocumulene-mediated annulation. *Tetrahedron*, 45(13), 4263 – 4286.
- Moseley, J. D., and Kappe, C. O. (2011). Green Chemistry A critical assessment of the greenness and energy efficiency of microwave-assisted organic synthesis. *The Royal Society of Chemistry*, 13, 794–806.
- Mourad, AF. E., Aly, A. A., Farag, H. H., and Beshr, E. A. (2007). Microwave assisted synthesis of triazoloquinazolinones and benzimidazoquinazolinones. *Beilstein Journal of Organic Chemistry*, 3(11), 1–5.
- Mukherjee, M., Sen, B., Pal, S., Banerjee, S., Lohar, S., Zangrando, E., and Chattopadhyay, P. (2015). RSC Advances. *RSC Advance*, 1–8.
- Mut-Salud, N., Álvarez, P. J., Garrido, J. M., Carrasco, E., Aránega, A., and R.-S. F. (2016). Antioxidant Intake and Antitumor Therapy: Toward Nutritional

Recommendations for Optimal Results. *Oxidative Medicine and Cellular Longevity*, 1–19.

Najafi, M., Mood, H., K., Zahedi, M., And Klein, E. (2011). DFT / B3LYP study of the substituent effect on the reaction enthalpies of the individual steps of single electron transfer – proton transfer and sequential proton loss electron transfer mechanisms of chroman derivatives antioxidant action. *Computational and Theoretical Chemistry*, 969, 1–12.

Naveen, S., Anandanwar, S. M., Prasad, J. S., Gayathri, V., and Bhattacharjee, R. (2006). Synthesis and Crystal Structure of 6-Butyl-5, 6-dihydrobenzo- [4 , 5] imidazo [1 , 2- c] quinazoline. *Analytical Sciences*, 22, 185–186.

Negi, A., Alex J. M., Amrutkar S. M., Baviskar A. T., Joshi, G., Singh, S. Banerjee, U. C., and Kumar, R. (2015). Imine/amide–imidazole conjugates derived from 5-amino-4-cyano- N1-substituted benzyl imidazole: Microwave-assisted synthesis and anticancer activity via selective topoisomerase-II-a inhibition. *Bioorg Med Chem.*23, 5654-5661.

Niu, H., Wang, W., Li, J., Lei, Y., Zhao, Y., Yang, W., Zhao, C., Lin, B., Song, S., and Wang, S. (2017). A novel structural class of coumarin-chalcone fibrates as PPAR α / γ agonists with potent antioxidant activities: Design , synthesis , biological evaluation and molecular docking studies. *European Journal of Medicinal Chemistry*, 138, 212–220.

Oliveira, S., Souza, G. A., Eckert, C. R., Silva, T. A., Sobral, E. S., Fávero, O. A., & Ferreira, M. J. P., Romoff, P., and B. W. J. (2014). Evaluation of Antiradical Assaya used in Determining the Antioxidant Capacity of Pure Compounds and Plant Extracts. *Quim. Nova*, 37(3), 497–503.

Omar, S. A. (2014). *Synthesis, Characterization and Biological Activities of Tridentatenns Schiff Bases and Thier Copper (II) Complexes Containing Saccharin*.

Pang, X., Chen, C., Li, M., & and Xi, C. (2015). A concise and efficient synthesis of benzimidazo [1 , 2- c] quinazolines through CuI-catalyzed intramolecular N-arylations. *Beilstein J. Org. Chem.*, 11, 2365–2369.

Parshad, B., Duraisamy, A. J., Saini, S., Yadav, P., Vats, P., and KS., S. (2016). Synthesis and SAR Study of Antioxidant Potential of Polyhydroxy Coumarin Derivatives. *Medicinal Chemistry*, 6(7), 506–514.

Pavia, D. L., Lampman, G. M., and Kriz, G. S. (2009). *Introduction to Spectroscopy* (forth edit.). Belmont: Brooks/ Cole.

Pellegrini, N., Rio, D. D., Colombi, B., Bianchi, M., and Brighenti, F. (2003). Application of the 2 , 2 ' -Azinobis (3-ethylbenzothiazoline-6-sulfonic acid) Radical Cation Assay to a Flow Injection System for the Evaluation of Antioxidant Activity of Some Pure Compounds and Beverages. *J. Agric. Food*

Chem, 51, 260–264.

Peng, Z. (2012). *Heat Transfer in Microwave Heating*.

Pessoa-Mahana, H., Pessoa-Mahana, C. D., Salazar, R., Valderrama, J. A., Saez, E., and Araya-Maturana, R. (2004). Solvent-Free Synthesis of 6-Arylbenzimidazo [1, 2- c] quinazolines under Microwave Irradiation. *Synthesis*, (3), 436–440.

Petrova, O. N., Zamigajlo, L. L., Ostras, K. S., Shishkina, S. V., Shishkin, O. V., Borisov, A. V., Musatov, V. I., Shirobokova, M. G., A., & Lipson, V. V. (2015). Multicomponent reaction of 2 - aminobenzimidazole , arylglyoxals , and 1 , 3 - cyclohexanedione. *Chem. Heterocycl. Compd.*, 51(4), 310–319.

Polshettiwar, V., and Varma, R. (2010). Fundamentals of Aqueous Microwave Chemistry. In *Aqueous Microwave Assisted Chemistry: Synthesis and Catalysis* (pp. 1–10).

Rahmani, Z, Pordel, M., and D. A. (2014). Design , Synthesis , Fluorescence Properties and Antibacterial Activities of New 8-Chloro-3-Alkyl-3 H -Pyrazolo [4 , 3- a] acridine-11-Carbonitriles. *Bull. Korean Chem. Soc.*, 35(2), 551–556.

Rajput, R., and Mishra, A. P. (2012). A review on Biological Activity of Quinazolines. *International Journal of Pharmaceutical Sciences*, 4(2), 66–70.

Rakesh, K. P., Manukumar, H. M., and Gowda, D. C. (2015). Schiff"s bases of quinazolinone derivatives: Synthesis and SAR studies of a novel series of potential anti-inflammatory and antioxidants. *Bioorganic & Medicinal Chemistry Letters*, 25, 1072–1077.

Re, R., Pellegrini, N., Proteggente, A., Pannala, A. Yang, M., and Rice-Evans, C. (1999). Antioxidant Activity Applying an Improved ABTS Radical Ction Decolorization Assay. *Free Radical Biology & Medicine*, 26(9/10), 1231–1237.

Rohini, R., Shanker, K., Reddy, P. M., & Ravinder, V. (2010). Synthesis and Antimicrobial Activities of a New Class of 6-Arylbenzimidazo[1,2-c]quinazolines. *J. Braz. Chem. Soc.*, 21(1), 49–57.

Rohini, R., Shanker, K., Reddy, P. M., Ho, Y-P., and Ravinder, V. (2009). Mono and bis-6-arylbenzimidazo[1,2-c]quinazolines: A new class of antimicrobial agents. *European Journal of Medicinal Chemistry*, 44, 3330–3339.

Saha, B., Sharma, S., and Kundu, B. (2007). Efficient Method for the Synthesis of Benzimidazoquinazoline Derivatives with Three - Point Diversity. *Synthetic Communications*, 37, 3455–3470.

Sahar, A., Khan, Z. A., Ahmad, M., Zahoor, A. F., Mansha, A., and Iqbal, A. (2017). Synthesis and antioxidant potential of some biscoumarin derivatives. *Tropical Journal of Pharmaceutical Research*, 16(1), 203–210.

- Salahuddin , Shaharyar, M., and Mazumder, A. (2012). Benzimidazoles : A biologically active compounds. *Arabian Journal of Chemistry*.
- Saluja, P., Sharma, H., Kaur, N., Singh, N., Jang, D. O. (2012). Benzimidazole-based imine-linked chemosensor: Chromogenic sensor for Mg ²⁺ and fluorescent sensor for Cr ³⁺. *Tetrahedron*, 68, 2289–2293.
- Sarikaya, S. B. O. (2015). Acetylcholinesterase inhibitory potential and antioxidant properties of pyrogallol. *Journal of Enzyme Inhibition and Medicinal Chemistry*, 30(5), 761–766.
- Selvam, T. P., and Kumar, P. V. (2011). Quinazoline Marketed drugs – A Review Quinazoline Marketed drugs – A Review. *Research in Pharmacy*, 1(1), 1–21.
- Shakhathreh, M. A., Al-Smadi, M. L., Khabour, O. F., Shuaibu, F. A., Hussein, E. I., and Alzoubi, K. H. (2016). Study of the antibacterial and antifungal activities of synthetic benzyl bromides , ketones , and corresponding chalcone derivatives. *Drug Design Development and Therapy*, 10, 3653–3660.
- Shalaby, E. A., and Shanab, S. M. M. (2013). Antioxidant compounds , assays of determination and mode of action. *African Journal of Pharmacy and Pharmacology*, 7(10), 528–539. doi:10.5897/AJPP2013.
- Sheldrick, G. M. (1996a). SAINT, V4: Software reference manual Siemens analytical X-ray systems. Madison, WI, USA.
- Sheldrick, G. M. (1996b). SADABS, Program for empirical absorption correction of area detector data. University of Göttingen, Göttingen, Germany.
- Sheldrick, G. M. (1997). SHELXTL-97 V5. 10. Bruker AXS Inc., Madison, WI-53719, USA.
- Shen, C., Wang, L., Wen, M., Shen, H., Jin, J., and Zhang, P. (2016). Synthesis of Benzimidazo[1,2 - c]quinazolines via Metal-Free Intramolecular C – H Amination Reaction. *Industrial & Engineering Chemistry Research*, A–E.
- Shirini, F., Safarpour, M., Langarudi, N., Daneshvar, N., Mashhadinezhad, M., & Nabinia, N. (2017). Preparation of a new DABCO-based ionic liquid and investigation on its application in the synthesis of benzimidazoquinazolinone and pyrimido[4,5-b]-quinoline derivatives. *Journal of Molecular Liquids*, 1–30.
- Shri, C. N., Aruna, A., and Vetrichelvan, T. (2015). Synthesis of 6-Aryl Benzimidazo [1 , 2-c] Quinazoline Derivatives and Their Antimicrobial Evaluation. *International Journal of Scientific Research*, 4(8), 713–714.
- Singh, N., Pandurangan, A., Rana, K., Anand, P., Ahamad, A., & Tiwari, A., K. (2012). Benzimidazole : A short review of their antimicrobial activities. *International Current Pharmaceutical Journal*, 1(5), 119–127.

- Singh, P., Kumar, R., Tiwari, S., Khanna, R. S., Tewari, A. k., and Khanna, H. D. (2015). Docking , Synthesis and Evaluation of Antioxidant Activity of 2,4,5-Triaryl Imidazole. *Clinical & Medical Biochemistry*, 1(1), 2–5.
- Sipos, A., Máté, G., Roth, E., Borbás, A., Batta, G., Bereczki, I., Kéki, S., Jóna, I., Ostorházi, E., Rozgonyi, F., Vanderlinden, E., N., & L., and Herczegh, P. (2012). European Journal of Medicinal Chemistry Synthesis of fl uorescent ristocetin aglycon derivatives with remarkable antibacterial and antiviral activities. *European Journal of Medicinal Chemistry*, 58, 361–367.
- Spek, A. L. (2009). Structure validation in chemical crystallography. *Acta Crystallographica Section D*, 65, 148–155.
- Subhashini, N. J. S. and Hanumanthu, P. (2001). Azlactones in heterocyclic synthesis : Part IV-A new route for the synthesis of 6-substituted and 6-arylidene-benzimidazo- [1 ,2-c]quinazolines. *Indian Journal of Chemistry*, 40B(May), 430–432.
- Tajammal , A., Batool , M., Ramzan , A., Samra , M. M., Mahnoor , I., Verpoort, F., Irfan, A., Al-Sehemi , A. G., Munawar, A. M., and Basra, M. A. R. (2017). Synthesis , antihyperglycemic activity and computational studies of antioxidant chalcones and fl avanones derived from 2 , 5 dihydroxyacetophenone. *Journal of Molecular Structure Journal*, 1148, 512–520.
- Tana, W., Li, Q., Zhou, T., Chen, Q., Wang, G., Dong, F., and Guo, Z. (2017). Synthesis and antioxidant ability of 6,60-diamino-6,60-dideoxytrehalose. *Bioorganic Chemistry*, 74, 66–71.
- Tang, F., Wang, C., Wang, X., and Li, L. (2015). Facile Synthesis of Biocompatible Fluorescent Nanoparticles for Cellular Imaging and Targeted Detection of Cancer Cells. *Applied Material and Interfaces*, 1–22.
- Tang, L., and Cai, M. (2012). A highly selective and sensitive fluorescent sensor for Cu 2 + and its complex for successive sensing of cyanide via Cu 2 + displacement approach. *Sensors & Actuators: B. Chemical*, 173, 862–867.
- Tang, L., Zhou, P., Zhong, K., Hou, S. (2013). Fluorescence relay enhancement sequential recognition of Cu²⁺ and CN[–] by a new quinazoline derivative. *Sensors and Actuators B*, 182, 439– 445.
- Thirupathaiah, A., Dasharatham, D. (2012). An Efficient Synthesis of Schiff Bases Containing Benzimidazole Moiety Catalyzed by Bismuth Trichloride Under Microwave Irradiation. *Oriental Journal of Chemistry*, 28(1), 575–579.
- Vats, P., Hadjimitova, V., Yoncheva, K., Kathuria, A., Sharma, A., Chand, K., Duraisamy, A. J., Sharma, A. K., Sharma, A. K. Saso, L., and S. S. K. (2014). Chromenone and quinolinone derivatives as potent antioxidant agents. *Med Chem Res*, 44, 1–8.

- Ventola, C. L. (2015). The Antibiotic Resistance Crisis Part 1 : Causes and Threats. *P&T*, 40(4), 277–283.
- Vernekar, V. U., Hosamani, K. M., Shaikh, I. N., and Achar, K. C. (2011). PTA ($\text{H}_3\text{PO}_4 \cdot 12\text{WO}_3 \cdot x\text{H}_2\text{O}$): An eco-friendly catalyst for the synthesis of new Schiff-bases containing benzimidazole moiety. *Arabian Journal of Chemistry*.
- Via, L. D., Gia, O., Magno, S. M., Settimo, A. D., Marini, A. M., Primofiore, G., Settimo, F. D., and Salerno, S. (2001). Synthesis , in vitro antiproliferative activity and DNA-interaction of benzimidazoquinazoline derivatives as potential anti-tumor agents. *Il Farmaco*, 56, 159–167.
- Walston, J. (2018). Antioxidant and cancer.
- Wang, D., and Gao, F. (2013). Quinazoline derivatives : synthesis and bioactivities. *Chemistry Central Journal*, 7(95), 1–15.
- Wang, Q., and Zhou, H. (2017). Ammonium Arylspiroborate Compounds : Synthesis , Crystal Structure , Fluorescence Properties , and Antibacterial Activity. *Organometallics*.
- Xu, S., Lu, J., and Fu, H. (2011). Copper-catalyzed cascade synthesis of benzimidazoquinazoline derivatives under mild condition. *Chem. Commun*, 47, 5596–5598.
- Yerragunta, V., patil, P., Srujana, S., Devi, R., Gayathri, R., Srujana, and Divya, A. (2014). Benzimidazole Derivatives and Its Biological Importance : A Review. *PharmaTutor Magazine*, 2(3), 109–113.
- Yong, Y., Xiao-li, Y., Xue-gang, L., Jing, Z., Baoshun, Z., and Lujiang, Y. (2007). Synthesis and Antimicrobial Activity of 8-Alkylberberine Derivatives with a Long Aliphatic Chain. *Etter...Planta Med*, 73, 602–604. doi:10.1055/s-2007-967180
- Zayed, M. F., and Hassan, M. H. (2014). Synthesis and biological evaluation studies of novel quinazolinone derivatives as antibacterial and anti-inflammatory agents. *Saudi Pharmaceutical Journal*, 22, 157–162.
- Zhang, M., Dai, ZC., Qian, SS., Liu, JY., Xiao, Y., Lu, AM., Zhu, HL., Wang, JX., and Ye, Y. (2014). Design, Synthesis, Antifungal, and Antioxidant Activities of (E) - 6-((2- Phenylhydrazono)methyl)quinoxaline Derivatives. *Journal of Agricultural and Food Chemistry*, 62, 9637–9643.
- Zhang, Y., Fang, Y., Liang, H., Wang, H., Hu, K., Liu, X., Yi, X., and Peng, Y. (2013). Synthesis and antioxidant activities of 2-oxo-quinoline-3-carbaldehyde Schiff-base derivatives. *Bioorganic & Medicinal Chemistry Letters*, 23, 107–111.