

DESIGN, SYNTHESIS OF FLAVOKAWAIN B  
DERIVATIVE AND THEIR CYTOTOXIC  
EFFECTS ON MCF-7 AND MDA-MB-231 CELL  
LINES

ADDILA BINTI ABU BAKAR

Master of Science

UNIVERSITI MALAYSIA PAHANG



## **SUPERVISOR'S DECLARATION**

We hereby declare that we have checked this thesis and in our opinion, this thesis is adequate in terms of scope and quality for the award of the degree of Master of Science.

---

(Supervisor's Signature)

Full Name : DR. MUHAMMAD NADEEM AKHTAR

Position : ASSOCIATE PROFESSOR

Date :

---

(Co-supervisor's Signature)

Full Name : DR. SAIFUL NIZAM BIN TAJUDDIN

Position : ASSOCIATE PROFESSOR

Date :



## **STUDENT'S DECLARATION**

I hereby declare that the work in this thesis is based on my original work except for quotations and citation which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at Universiti Malaysia Pahang or any other institutions.

---

(Student's Signature)

Full Name : ADDILA BINTI ABU BAKAR

ID Number : MKD15002

Date :

DESIGN, SYNTHESIS OF FLAVOKAWAIN B DERIVATIVE AND THEIR  
CYTOTOXIC EFFECTS ON MCF-7 AND MDA-MB-231 CELL LINES

ADDILA BINTI ABU BAKAR

Thesis submitted in fulfillment of the requirements  
for the award of the degree of  
Master of Science

Faculty of Industrial Sciences and Technology  
UNIVERSITI MALAYSIA PAHANG

2018

## ACKNOWLEDGEMENT

First and foremost, I am very grateful to God the Almighty, the Most Gracious and the Most Merciful for giving me this chance and guiding me through.

I am extremely grateful and would like to express my sincere gratitude to my supervisor, Assoc. Prof. Dr. Muhammad Nadeem Akhtar for his creative ideas, invaluable guidance, continued encouragement, constant support and time spent in making this project possible.

I would also like to express my sincere gratitude to my Co-supervisor, Assoc. Prof. Dr. Saiful Nizam bin Tajuddin for his guidance, constant support and encouragement throughout this project.

I would like to express my sincere appreciation towards my colleague, Siti Noor Hajar binti Zamrus for her continued support and motivation throughout my research project. I would also like to thank all administrative and laboratory staff of Faculty of Industrial Sciences & Technology for their enormous help in any way needed to complete this research project.

I am very thankful to Assoc. Prof. Dr. Noorjahan Banu Alitheen, and her master's students, Nurul Fattin binti Che Rahim, Muhammad Nazirul Mubin bin Aziz and Yazmin binti Hussin from Faculty of Biotechnology and Biomolecular Science, Universiti Putra Malaysia for their generous help, particularly in the study of biological activities.

I would also like to express my gratitude to Dr. Seema Zareen as well as Universiti Malaysia Pahang and Ministry of Higher Education for their trust and financial support, which have helped me completing my master's degree.

Last but not least, I am grateful to my parents for their understanding, financial support and prayers. My appreciation also goes to everyone who has either directly or indirectly involved in this project.

## TABLE OF CONTENT

<b>DECLARATION</b>	
<b>TITLE PAGE</b>	<b>i</b>
<b>ACKNOWLEDGEMENT</b>	<b>ii</b>
<b>ABSTRAK</b>	<b>iii</b>
<b>ABSTRACT</b>	<b>iv</b>
<b>TABLE OF CONTENT</b>	<b>v</b>
<b>LIST OF TABLES</b>	<b>xi</b>
<b>LIST OF FIGURES</b>	<b>xiii</b>
<b>LIST OF SYMBOLS</b>	<b>xx</b>
<b>LIST OF ABBREVIATIONS</b>	<b>xxi</b>
<b>CHAPTER 1 INTRODUCTION</b>	<b>1</b>
1.1 Background of Research	1
1.2 Problem Statement	2
1.3 Objectives	3
1.4 Scope of Study	3
<b>CHAPTER 2 LITERATURE REVIEW</b>	<b>5</b>
2.1 Overview of Chalcone	5
2.2 Synthesis of Chalcone	5
2.2.1 Claisen-Schmidt Condensation Method	5
2.2.2 Acid Catalyzed Aldol Reaction	7

2.2.3	Microwave Irradiation Method	8
2.2.4	Synthesis of Chalcone by Using Boron Trifluoride Etherate	8
2.2.5	Palladium-Catalyzed Chalcone Synthesis	9
2.2.6	Suzuki Coupling Reaction	11
2.3	Pharmacological Activities of Chalcones	12
2.3.1	Anti-cancer Properties	14
2.3.2	Anti-oxidant Properties	17
2.3.3	Anti-inflammatory Properties	20
2.3.4	Anti-bacterial Properties	22
2.3.5	Anti-leishmanial Properties	26
2.3.6	Anti-malarial Properties	29
2.3.7	Immunosuppressive Activity of Chalcone	30
2.3.8	Anti-proliferative Properties	31
2.4	Structure-Activity Relationship of Chalcone	33
2.5	Breast Cancer	35
<b>CHAPTER 3 RESEARCH METHODOLOGY</b>		<b>38</b>
3.1	Synthesis of Flavokawain B Derivative ( <b>2, 4, 5, 44, 46, 75-91</b> ) by Claisen-Schmidt Condensation	38
3.2	Acetylation of 4-hydroxy-3-methoxybenzaldehyde	39
3.3	Purification of Flavokawain B Derivative	40
3.3.1	Column Chromatography	40

3.3.2	Thin Layer Chromatography Analysis	40
3.3.3	Crystallization	40
3.4	Percentage Yield	41
3.5	Characterization of Flavokawain B Derivative	41
3.5.1	Ultraviolet-Visible Spectroscopy Analysis	41
3.5.2	Fourier Transform Infrared Spectroscopy Analysis	42
3.5.3	Gas Chromatography-Mass Spectroscopy Analysis	42
3.5.4	Nuclear Magnetic Resonance Spectroscopy Analysis	43
3.6	Cytotoxic Effects of Synthetic Flavokawain B Derivative	43
3.6.1	Preparation of Cell Line	43
3.6.2	Preparation of Stock Solution of Flavokawain B Derivative	44
3.6.3	Determination of Cell Viability by 3-(4,5-dimethylthiazol-2-yl)- 2,5-diphenyltetrazolium bromide (MTT) Assay	44
3.7	Flow Chart of Research Activities	45
<b>CHAPTER 4 RESULTS &amp; DISCUSSION</b>		<b>46</b>
4.1	Characterization of Synthesized Flavokawain B Derivative ( <b>2, 4, 5, 44, 46, 75-91</b> )	46
4.1.1	( <i>E</i> )-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)-3-phenylprop-2-en-1-one ( <b>4</b> )	46
4.1.2	( <i>E</i> )-1-(2'-hydroxyl-4', 6'-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one ( <b>5</b> )	50
4.1.3	( <i>E</i> )-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)-3-(4-(methylthio)phenyl)prop-2-en-1-one ( <b>75</b> )	56



4.1.4	( <i>E</i> )-3-(2,3-dimethoxyphenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>76</b> )	59
4.1.5	( <i>E</i> )-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-en-1-one ( <b>77</b> )	63
4.1.6	( <i>E</i> )-3-(2,4-dimethoxyphenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>78</b> )	66
4.1.7	( <i>E</i> )-3-(2-chlorophenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>79</b> )	70
4.1.8	( <i>E</i> )-3-(2-fluorophenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>80</b> )	74
4.1.9	( <i>E</i> )-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one ( <b>81</b> )	77
4.1.10	( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	81
4.1.11	( <i>E</i> )-3-(3,5-dimethoxyphenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>83</b> )	88
4.1.12	( <i>E</i> )-3-(3-chlorophenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>84</b> )	91
4.1.13	( <i>E</i> )-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	94
4.1.14	( <i>E</i> )-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one ( <b>44</b> )	99
4.1.15	( <i>E</i> )-3-(4-bromophenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>86</b> )	102
4.1.16	( <i>E</i> )-3-(4-chlorophenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>87</b> )	105

4.1.17	( <i>E</i> )-3-(4-fluorophenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>46</b> )	111
4.1.18	( <i>E</i> )-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)-3-(p-tolyl)prop-2-en-1-one ( <b>88</b> )	114
4.1.19	( <i>E</i> )-3-(4-hydroxy-3-methoxyphenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>89</b> )	117
4.1.20	( <i>E</i> )-3-(4-(dimethylamino)phenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>2</b> )	120
4.1.21	( <i>E</i> )-3-(5-bromo-2-hydroxyphenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>90</b> )	124
4.1.22	( <i>E</i> )-3-(2-bromo-3-hydroxy-4-methoxyphenyl)-1-(2'-hydroxy-4', 6'-dimethoxyphenyl)prop-2-en-1-one ( <b>91</b> )	127
4.2	Cytotoxic Effects of Flavokawain B Derivative against MCF-7 and MDA-MB-231 Breast Cancer Cell Line	132
<b>CHAPTER 5 CONCLUSION</b>		<b>135</b>
5.1	General Conclusion	135
5.2	Recommendation	136
<b>REFERENCES</b>		<b>137</b>
<b>APPENDIX A1</b>		<b>148</b>
<b>APPENDIX A2</b>		<b>149</b>
<b>APPENDIX A3</b>		<b>150</b>
<b>APPENDIX A4</b>		<b>151</b>
<b>APPENDIX A5</b>		<b>152</b>
<b>APPENDIX A6</b>		<b>153</b>

<b>APPENDIX A7</b>	<b>154</b>
<b>APPENDIX A8</b>	<b>155</b>
<b>APPENDIX A9</b>	<b>156</b>
<b>APPENDIX A10</b>	<b>157</b>
<b>APPENDIX A11</b>	<b>158</b>
<b>APPENDIX B</b>	<b>159</b>
<b>APPENDIX C</b>	<b>160</b>

## LIST OF TABLES

Table 4.1	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-phenyl-prop-2-en-1-one ( <b>4</b> )	48
Table 4.2	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one ( <b>5</b> )	53
Table 4.3	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(4-(methylthio)phenyl)prop-2-en-1-one ( <b>75</b> )	58
Table 4.4	NMR data of ( <i>E</i> )-3-(2,3-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>76</b> )	62
Table 4.5	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-en-1-one ( <b>77</b> )	65
Table 4.6	NMR data of ( <i>E</i> )-3-(2,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>78</b> )	69
Table 4.7	NMR data of ( <i>E</i> )-3-(2-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>79</b> )	73
Table 4.8	NMR data of ( <i>E</i> )-3-(2-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>80</b> )	76
Table 4.9	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one ( <b>81</b> )	80
Table 4.10	NMR data of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	84
Table 4.11	Crystal parameters and data for structure refinement of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	85
Table 4.12	NMR data of ( <i>E</i> )-3-(3,5-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>83</b> )	90
Table 4.13	NMR data of ( <i>E</i> )-3-(3-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>84</b> )	93
Table 4.14	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	97
Table 4.15	Crystal parameters and data for structure refinement of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	98
Table 4.16	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one ( <b>44</b> )	101
Table 4.17	NMR data of ( <i>E</i> )-3-(4-bromophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>86</b> )	104
Table 4.18	NMR data of ( <i>E</i> )-3-(4-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>87</b> )	108
Table 4.19	NMR data of ( <i>E</i> )-3-(4-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>46</b> )	113

Table 4.20	NMR data of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-( <i>p</i> -tolyl)prop-2-en-1-one ( <b>88</b> )	116
Table 4.21	NMR data of ( <i>E</i> )-3-(4-hydroxy-3-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>89</b> )	120
Table 4.22	NMR data of ( <i>E</i> )-3-(4-(dimethylamino)phenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>2</b> )	123
Table 4.23	NMR data of ( <i>E</i> )-3-(5-bromo-2-hydroxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>90</b> )	126
Table 4.24	NMR data of ( <i>E</i> )-3-(2-bromo-3-hydroxy-4-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>91</b> )	130
Table 4.25	IC <sub>50</sub> values of flavokawain B derivative against MCF-7 and MDA-MB-231 cell line	132

## LIST OF FIGURES

Figure 2.1	Synthesis of chalcone via Claisen-Schmidt condensation	6
Figure 2.2	Mechanism in synthesis of chalcone via base catalyst Claisen-Schmidt condensation	6
Figure 2.3	Chalcones derivatives ( <b>1-3</b> ) synthesized via Claisen-Schmidt condensation method	7
Figure 2.4	Synthesis of chalcones via Aldol reaction with acid catalyst	8
Figure 2.5	Synthesis of chalcone derivatives by using microwave irradiation	8
Figure 2.6	Examples of chalcone derivatives synthesized by using Boron trifluoride etherate	9
Figure 2.7	Cross-coupling reaction of alkenylboronic acids with acid chlorides	9
Figure 2.8	Cross-coupling reaction of Arylboronic acids with Acid chlorides	9
Figure 2.9	General reaction of 3-Benzoylacrylic acid with Arylboronic acid or Aryl halides	10
Figure 2.10	Cross-coupling reaction of Benzoyl chlorides with Potassium styryltrifluoroborate	11
Figure 2.11	Pathway A, Coupling between activated Cinnamic acids and Phenylboronic acids	11
Figure 2.12	Pathway B, Coupling between activated Benzoic acids and Phenylvinylboronic acids	12
Figure 2.13	Natural chalcone flavokawain B ( <b>4</b> ), A ( <b>5</b> ) and C ( <b>6</b> ) from kava-kava plant	14
Figure 2.14	Bifendate-chalcone hybrid as permeability-glycoprotein (P-gp) and breast cancer resistance protein BCRP inhibitor	15
Figure 2.15	Dihalogenated chalcones and dienone derivative that inhibit tubulin polymerization, stabilize the tubulin and exhibit cytotoxicity against RPMI 8226 (myeloma), CCRF-CEM (leukemia), U937-GTB (lymphoma) and NCI-H69 (small-cell lung cancer) cell line	16
Figure 2.16	Chalcones linked imidazolones with potent anti-cancer activity towards cancer cell lines derived from leukemia, lung, colon, central nervous system (CNS), melanoma, ovarian, renal, prostate and breast cancer and exhibited cell cycle arrest at G2/M phase	17
Figure 2.17	Potent chalcone derivative with selective cytotoxicity against MCF-7 cancer cell and induced cell death by apoptosis	17
Figure 2.18	Compound <b>17</b> and <b>18</b> with promising anti-oxidant activity compared with standard Vitamin C, determined through DPPH free radical scavenging method	19
Figure 2.19	Methoxy and hydroxy substituted chalcone with comparable anti-oxidant activity with standard molecule $\alpha$ -topocole, evaluated by DPPH free radical scavenging activity, nitric oxide scavenging and PhNHNH <sub>2</sub> assay	19

Figure 2.20	Chalcone derivative ( <b>20</b> ) with potent anti-oxidant properties in comparison with standard anti-oxidant BHA	19
Figure 2.21	Chalcone with effective anti-inflammatory activity in NO scavenging activity	20
Figure 2.22	Chalcone with strong inhibition activity against nitrite production	21
Figure 2.23	Chalcone derivatives with inhibitory activity against NO accumulation in RAW 264.7 cells	22
Figure 2.24	Chalcone with anti- <i>Staphylococcus aureus</i> effects	23
Figure 2.25	Chalcone with potent anti-bacterial activity screened against <i>Escherichia coli</i> and <i>Pseudomonas aeruginosa</i>	25
Figure 2.26	Hybrid chalcone with potent anti-bacteria properties than standard norfloxacin against <i>Staphylococcus aureus</i> with minimum inhibitory concentration value of 2 µg/mL	25
Figure 2.27	Compound with potent anti-bacterial activity against <i>Bacillus subtilis</i> , <i>Pseudomonas species</i> , <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> compared to ampicillin	26
Figure 2.28	Chalcone with anti-leishmanial activity against promastigotes and intracellular amastigotes of <i>Leishmanial amazonensis</i>	27
Figure 2.29	Chalcone <b>47-56</b> with potent <i>in vitro</i> anti-leishmanial activity against extracellular promastigote and intracellular amastigote of <i>Leishmanial donovani</i>	28
Figure 2.30	Chalcone with anti-malarial activity against D10 and W2 strains of <i>Plasmodium falciparum</i>	29
Figure 2.31	Chalcone derivatives with anti-malarial activity against <i>P. falciparum</i> 3D7 strain	30
Figure 2.32	Chalcone with potent immunosuppressive activity	31
Figure 2.33	Conjugated chalcone and azaserumbone derivatives with 1-ethylene-4-methylene-1,2,3-triazole linker with potent anti-proliferative activity	32
Figure 2.34	Chemical compound that promote apoptotic cell death in human hepatoma cell	33
Figure 2.35	Compound with effective inhibitory activity against ABCG2	33
Figure 2.36	Hydroxychalcone derivatives with potential to uncouple mitochondria	34
Figure 2.37	Halogenated chalcone with potent anti-cancer activity	35
Figure 2.38	Mammogram of breast cancer	35
Figure 3.1	Scheme 1: Synthesis of flavokawain B derivative ( <b>2, 4, 5, 44, 46, 75-91</b> ) by Claisen-Schmidt condensation method	39
Figure 3.2	Scheme 2: General for acetylation of 4-hydroxy-3-methoxy-benzaldehyde	39

Figure 4.1	UV spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-phenylprop-2-en-1-one ( <b>4</b> )	47
Figure 4.2	IR spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-phenylprop-2-en-1-one ( <b>4</b> )	47
Figure 4.3	Structure of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-phenylprop-2-en-1-one ( <b>4</b> )	48
Figure 4.4	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-phenylprop-2-en-1-one ( <b>4</b> )	49
Figure 4.5	Mass fragmentation of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-phenylprop-2-en-1-one ( <b>4</b> )	50
Figure 4.6	UV spectrum of ( <i>E</i> )-1-(2'-hydroxyl-4',6'-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one ( <b>5</b> )	51
Figure 4.7	IR spectrum of ( <i>E</i> )-1-(2'-hydroxyl-4',6'-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one ( <b>5</b> )	52
Figure 4.8	Structure of ( <i>E</i> )-1-(2'-hydroxyl-4',6'-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one ( <b>5</b> )	53
Figure 4.9	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxyl-4',6'-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one ( <b>5</b> )	54
Figure 4.10	Mass fragmentation of ( <i>E</i> )-1-(2'-hydroxyl-4',6'-dimethoxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one ( <b>5</b> )	55
Figure 4.11	UV spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(4-(methylthio)phenyl)prop-2-en-1-one ( <b>75</b> )	56
Figure 4.12	IR spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(4-(methylthio)phenyl)prop-2-en-1-one ( <b>75</b> )	57
Figure 4.13	Structure of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(4-(methylthio)phenyl)prop-2-en-1-one ( <b>75</b> )	58
Figure 4.14	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(4-(methylthio)phenyl)prop-2-en-1-one ( <b>75</b> )	59
Figure 4.15	UV spectrum of ( <i>E</i> )-3-(2,3-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>76</b> )	60
Figure 4.16	IR spectrum of ( <i>E</i> )-3-(2,3-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>76</b> )	61
Figure 4.17	Structure of ( <i>E</i> )-3-(2,3-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>76</b> )	62
Figure 4.18	GC-MS spectrum of ( <i>E</i> )-3-(2,3-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>76</b> )	63
Figure 4.19	UV spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-en-1-one ( <b>77</b> )	64
Figure 4.20	IR spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-en-1-one ( <b>77</b> )	64



Figure 4.21	Structure of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-en-1-one ( <b>77</b> )	65
Figure 4.22	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-en-1-one ( <b>77</b> )	66
Figure 4.23	UV spectrum of ( <i>E</i> )-3-(2,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>78</b> )	67
Figure 4.24	IR spectrum of ( <i>E</i> )-3-(2,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>78</b> )	68
Figure 4.25	Structure of ( <i>E</i> )-3-(2,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>78</b> )	69
Figure 4.26	GC-MS spectrum of ( <i>E</i> )-3-(2,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>78</b> )	70
Figure 4.27	UV spectrum of ( <i>E</i> )-3-(2-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>79</b> )	71
Figure 4.28	IR spectrum of ( <i>E</i> )-3-(2-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>79</b> )	72
Figure 4.29	Structure of ( <i>E</i> )-3-(2-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>79</b> )	73
Figure 4.30	GC-MS spectrum of ( <i>E</i> )-3-(2-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>79</b> )	74
Figure 4.31	UV spectrum of ( <i>E</i> )-3-(2-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>80</b> )	75
Figure 4.32	IR spectrum of ( <i>E</i> )-3-(2-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>80</b> )	75
Figure 4.33	Structure of ( <i>E</i> )-3-(2-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>80</b> )	76
Figure 4.34	GC-MS spectrum of ( <i>E</i> )-3-(2-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>80</b> )	77
Figure 4.35	UV spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one ( <b>81</b> )	78
Figure 4.36	IR spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one ( <b>81</b> )	79
Figure 4.37	Structure of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one ( <b>81</b> )	80
Figure 4.38	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one ( <b>81</b> )	81
Figure 4.39	UV spectrum of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	82
Figure 4.40	IR spectrum of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	83

Figure 4.41	Structure of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	84
Figure 4.42	ORTEP diagram of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	85
Figure 4.43	GC-MS spectrum of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	86
Figure 4.44	Mass fragmentation of ( <i>E</i> )-3-(3,4-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>82</b> )	87
Figure 4.45	UV spectrum of ( <i>E</i> )-3-(3,5-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>83</b> )	88
Figure 4.46	IR spectrum of ( <i>E</i> )-3-(3,5-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>83</b> )	89
Figure 4.47	Structure of ( <i>E</i> )-3-(3,5-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>83</b> )	90
Figure 4.48	GC-MS spectrum of ( <i>E</i> )-3-(3,5-dimethoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>83</b> )	91
Figure 4.49	UV spectrum of ( <i>E</i> )-3-(3-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>84</b> )	92
Figure 4.50	IR spectrum of ( <i>E</i> )-3-(3-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>84</b> )	92
Figure 4.51	Structure of ( <i>E</i> )-3-(3-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>84</b> )	93
Figure 4.52	GC-MS spectrum of ( <i>E</i> )-3-(3-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>84</b> )	94
Figure 4.53	UV spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	95
Figure 4.54	IR spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	96
Figure 4.55	Structure of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	97
Figure 4.56	ORTEP diagram of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	97
Figure 4.57	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one ( <b>85</b> )	99
Figure 4.58	UV spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one ( <b>44</b> )	100
Figure 4.59	IR spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one ( <b>44</b> )	100
Figure 4.60	Structure of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one ( <b>44</b> )	101

Figure 4.61	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one ( <b>44</b> )	102
Figure 4.62	UV spectrum of ( <i>E</i> )-3-(4-bromophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>86</b> )	103
Figure 4.63	IR spectrum of ( <i>E</i> )-3-(4-bromophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>86</b> )	103
Figure 4.64	Structure of ( <i>E</i> )-3-(4-bromophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>86</b> )	104
Figure 4.65	GC-MS spectrum of ( <i>E</i> )-3-(4-bromophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>86</b> )	105
Figure 4.66	UV spectrum of ( <i>E</i> )-3-(4-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>87</b> )	106
Figure 4.67	IR spectrum of ( <i>E</i> )-3-(4-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>87</b> )	107
Figure 4.68	Structure of ( <i>E</i> )-3-(4-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>87</b> )	108
Figure 4.69	GC-MS spectrum of ( <i>E</i> )-3-(4-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>87</b> )	109
Figure 4.70	Mass fragmentation of ( <i>E</i> )-3-(4-chlorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>87</b> )	110
Figure 4.71	UV spectrum of ( <i>E</i> )-3-(4-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>46</b> )	111
Figure 4.72	IR spectrum of ( <i>E</i> )-3-(4-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>46</b> )	112
Figure 4.73	Structure of ( <i>E</i> )-3-(4-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>46</b> )	113
Figure 4.74	GC-MS spectra of ( <i>E</i> )-3-(4-fluorophenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>46</b> )	114
Figure 4.75	UV spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(p-tolyl)prop-2-en-1-one ( <b>88</b> )	115
Figure 4.76	IR spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(p-tolyl)prop-2-en-1-one ( <b>88</b> )	115
Figure 4.77	Structure of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(p-tolyl)prop-2-en-1-one ( <b>88</b> )	116
Figure 4.78	GC-MS spectrum of ( <i>E</i> )-1-(2'-hydroxy-4',6'-dimethoxyphenyl)-3-(p-tolyl)prop-2-en-1-one ( <b>88</b> )	117
Figure 4.79	UV spectrum of ( <i>E</i> )-3-(4-hydroxy-3-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>89</b> )	118
Figure 4.80	IR spectrum of ( <i>E</i> )-3-(4-hydroxy-3-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>89</b> )	119

Figure 4.81	Structure of ( <i>E</i> )-3-(4-hydroxy-3-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>89</b> )	120
Figure 4.82	UV spectrum of ( <i>E</i> )-3-(4-(dimethylamino)phenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>2</b> )	121
Figure 4.83	IR spectrum of ( <i>E</i> )-3-(4-(dimethylamino)phenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>2</b> )	122
Figure 4.84	Structure of ( <i>E</i> )-3-(4-(dimethylamino)phenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>2</b> )	123
Figure 4.85	GC-MS spectrum of ( <i>E</i> )-3-(4-(dimethylamino)phenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>2</b> )	124
Figure 4.86	UV spectrum of ( <i>E</i> )-3-(5-bromo-2-hydroxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>90</b> )	125
Figure 4.87	IR spectrum ( <i>E</i> )-3-(5-bromo-2-hydroxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>90</b> )	125
Figure 4.88	Structure of ( <i>E</i> )-3-(5-bromo-2-hydroxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>90</b> )	126
Figure 4.89	GC-MS spectrum of ( <i>E</i> )-3-(5-bromo-2-hydroxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>90</b> )	127
Figure 4.90	UV spectrum of ( <i>E</i> )-3-(2-bromo-3-hydroxy-4-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>91</b> )	128
Figure 4.91	IR spectrum of ( <i>E</i> )-3-(2-bromo-3-hydroxy-4-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>91</b> )	129
Figure 4.92	Structure of ( <i>E</i> )-3-(2-bromo-3-hydroxy-4-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>91</b> )	130
Figure 4.93	GC-MS spectrum of ( <i>E</i> )-3-(2-bromo-3-hydroxy-4-methoxyphenyl)-1-(2'-hydroxy-4',6'-dimethoxyphenyl)prop-2-en-1-one ( <b>91</b> )	131

## LIST OF SYMBOLS

s	Singlet
d	Doublet
t	Triplet
m	Multiplet
$J$	Coupling constant
W	Watt
MHz	Mega Hertz
mg/mL	Milligram per millilitre
U/mL	Unit per millilitre
$m/z$	Mass to charge ratio
$\mu\text{M}$	Micromolar
$\mu\text{g/mL}$	Microgram per millilitre
$\alpha$	Alpha
$\beta$	Beta
$\lambda_{\text{max}}$	Maximum wavelength
$\delta$	Delta

## LIST OF ABBREVIATIONS

$^{13}\text{C}$ -NMR	Carbon Nuclear Magnetic Resonance
$^1\text{H}$ -NMR	Proton Nuclear Magnetic Resonance
ABCG2	ATP-binding cassette sub-family G member 2
BCRP	Breast cancer resistance protein
$\text{BF}_3\text{-Et}_2\text{O}$	Boron trifluoride diethyl etherate
CC	Column chromatography
$\text{CDCl}_3$	Deuterated chloroform
$\text{CF}_3$	Trifluoromethyl
$\text{CO}_2$	Carbon dioxide
CuTC	Copper(I)-thiophene-2-carboxylate
DMEM	Dulbecco's Modified Eagle Medium
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
$\text{ED}_{50}$	Median effective dose
FBS	Fetal Bovine Serum
FTIR	Fourier Transform Infrared spectroscopy
GC-MS	Gas Chromatography-Mass Spectrometry
$\text{GI}_{50}$	50% growth inhibition
Hep-G2	Liver hepatocellular carcinoma
$\text{IC}_{50}$	Concentration for 50% inhibition
$\text{K}_2\text{CO}_3$	Potassium carbonate
KOH	Potassium hydroxide
LU	Lung adenocarcinoma
MCF-7	Human breast adenocarcinoma cell line
MDA-MB-231	Human breast adenocarcinoma cell line
MDR	Multi-drug resistance

MIC	Minimum inhibitory concentration
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NaOH	Sodium hydroxide
NMR	Nuclear Magnetic Resonance spectroscopy
OCH <sub>3</sub>	Methoxy
P338	Leukemia
PARP	Poly (ADP ribose) polymerase
PBS	Phosphate buffer saline
Pd	Palladium
Pd(dba) <sub>2</sub>	Bis(dibenzylideneacetone)palladium(0)
PdCl <sub>2</sub>	Palladium(II) chloride
p-gp	Permeability glycoprotein
PPh <sub>3</sub>	Triphenylphospine
RPMI	Roswell Park Medium Institute
S-CH <sub>3</sub>	Thio-methyl
SOCl <sub>2</sub>	Thionyl Chloride
SSG	Sodium stigliconate
SW480	Colon adenocarcinoma
TLC	Thin Layer Chromatography
UV-Vis	Ultraviolet-visible spectroscopy
VRP	Verapamil