

# **A PHYTOCHEMICAL AND PHARMACOLOGICAL STUDY OF TEN *COMMIPHORA* SPECIES INDIGENOUS TO SOUTH AFRICA**

---

**MARIA PENELOPE PARASKEVA**

**A DISSERTATION SUBMITTED TO THE FACULTY OF HEALTH SCIENCES, UNIVERSITY OF  
THE WITWATERSRAND, JOHANNESBURG IN FULFILMENT OF THE REQUIREMENTS FOR THE  
DEGREE OF MASTER OF PHARMACY**

**JANUARY, 2007**



## DECLARATION

---

I, Maria Penelope Paraskeva, declare that this dissertation is my own, unaided work except where acknowledged. It is being submitted in fulfilment for the degree of Master of Pharmacy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

.....

(Signature of Candidate)

..... day of ....., 2007

## ABSTRACT

---

*Commiphora* species (from which myrrh is obtained) has been a source of several novel and bio-active natural compounds. Traditionally, *Commiphora* (Burseraceae) is used in southern Africa for the treatment of ulcers, fevers, and as a remedy for snake and scorpion bites. In western Africa, the macerated stem is used in the treatment of rheumatic conditions. The resin of some *Commiphora* species is applied topically to aid in wound healing. Documented uses include antibacterial and antifungal properties, as well as cytotoxic, cytostatic and anti-oxidant activity. The botanical diversity of this genus in South Africa warrants a study of this plant group, to provide scientific evidence for the traditional use of *Commiphora* species in African healing rites.

Ten *Commiphora* species were investigated. Fresh plant material of the selected species were identified and collected from natural populations in the Limpopo Province. Active compounds, viz. kaempferol and dihydrokaempferol, in *C. glandulosa* (stem) were isolated using bioassay-guided fractionation and identified using nuclear magnetic resonance spectroscopy. The stem and leaf extracts of each species were analysed for *in vitro* anti-oxidant, antimicrobial, anti-inflammatory, anticancer activity, as well as cytotoxicity. The anti-oxidant activity of the extracts was investigated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay and the 2,2'-azino-bis(3-ethyl-benzthiazoline-6-sulfonic acid) (ABTS) assays. Extracts generally exhibited poor anti-oxidant activity in the DPPH assay, with the exception of *C. schimperi* (stem), *C. neglecta* (stem), *C. tenuipetiolata* (stem and leaf), and *C. edulis* (stem), which possessed  $IC_{50}$  values ranging between 7.31  $\mu\text{g/ml}$  and 10.81  $\mu\text{g/ml}$ . Isolated compounds were subjected to the DPPH assay to determine the anti-oxidant potential of each compound, separately and in combination to establish possible synergistic, antagonistic or additive effects. The flavonol, kaempferol ( $IC_{50} = 3.32 \mu\text{g/ml}$ ) showed exceptional radical scavenging activity, in contrast to the low activity displayed by dihydrokaempferol ( $IC_{50} = 301.57 \mu\text{g/ml}$ ), their combination being antagonistic. Greater anti-oxidant activity was observed for most species in the ABTS assay when compared to the results obtained in the DPPH assay. The best activity was observed for the stem extracts of *C. neglecta* ( $IC_{50} = 7.28 \mu\text{g/ml}$ ) and *C. mollis* ( $IC_{50} = 8.82 \mu\text{g/ml}$ ).

## ABSTRACT *continued*

---

*In vitro* antimicrobial efficacy was determined against Gram-positive and Gram-negative bacteria as well as yeasts using the MIC microtiter plate assay. A greater selectivity was exhibited by the extracts against the Gram-positive bacteria and yeast than against the Gram-negative bacteria. Using death kinetics studies (time-kill studies), the rate at which the antimicrobial agent kills pathogens over a 24-hour period was determined. The antibacterial activity of *Commiphora marlothii* (stem) was observed to begin at ca. 30 min of the exposure of *S. aureus* to the different concentrations of plant extract. All concentrations exhibited antibacterial activity, with a complete bactericidal effect achieved by all test concentrations by the 24<sup>th</sup> hour. *Commiphora pyracanthoides* (stem) displayed anti-inflammatory activity through good inhibition of the 5-LOX enzyme ( $IC_{50} = 27.86 \mu\text{g/ml}$ ).

The ability of extracts and kaempferol to inhibit the *in vitro* growth of three human cancer cell lines, namely the colon adenocarcinoma (HT-29), breast adenocarcinoma (MCF-7), and the neuronal glioblastoma (SF-268), was evaluated using the sulforhodamine (SRB) antiproliferative assay. The most active *Commiphora* species against the HT-29 cells were *C. glandulosa* (leaf and stem) and *C. marlothii* (leaf). The MCF-7 cell line was the most sensitive to indigenous *Commiphora* species, with *C. edulis* (leaf and stem), *C. glandulosa* (leaf and stem), *C. marlothii* (leaf), *C. pyracanthoides* (leaf and stem), *C. schimperi* (stem), and *C. viminea* (stem) all possessing an inhibition greater than 80% at 100  $\mu\text{g/ml}$ . *Commiphora glandulosa* (leaf and stem) and *C. pyracanthoides* (leaf and stem) were the two most active species against the SF-268 cells, with  $IC_{50}$  values ranging between 68.50  $\mu\text{g/ml}$  and 71.45  $\mu\text{g/ml}$ . The inhibition of the cancer cell proliferation by kaempferol in all three-cancer cell lines was determined, with  $IC_{50}$  values of 9.78  $\mu\text{g/ml}$  in HT-29 cells, 20.21  $\mu\text{g/ml}$  in MCF-7 cells and 43.83  $\mu\text{g/ml}$  in SF-268 cells. The microculture tetrazolium cellular viability (MTT) assay was used to determine the cellular toxicity of the extracts against transformed human kidney epithelium (Graham) cells. *Commiphora glandulosa* (stem) proved to be most toxic ( $IC_{50} = 30.5 \mu\text{g/ml}$ ). The  $IC_{50}$  values for all other extracts were in excess of 95  $\mu\text{g/ml}$  suggesting low *in vitro* toxicity for the majority of the species.

## **ABSTRACT *continued***

---

A phytochemical investigation of the non-volatile constituents of the leaf and stems was conducted using high performance liquid chromatography (HPLC). The HPLC profiles and UV spectra of the stem extracts, and the representative flavonoid patterns in the leaf extracts of the species indicate that a similarity exists in their chemical fingerprint.

## PRESENTATIONS

---

M. Paraskeva, A.M. Viljoen, S.F. van Vuuren, H. Davids and R.L. van Zyl, 2005. The pharmacological activity of 10 species of *Commiphora* indigenous to South Africa. Podium presentation, 5<sup>th</sup> Annual Meeting of the Indigenous Plant Use Forum (IPUF). Grahamstown, 27-30 June 2005. (Abstract in Appendix C)

M. Paraskeva, A.M. Viljoen, S.F. van Vuuren, H. Davids and R.L. van Zyl, 2005. The biological activity of 10 species of *Commiphora* indigenous to South Africa. Podium presentation at the University of Johannesburg Post Graduate Symposium. Johannesburg, 2 November 2005 (Abstract in Appendix C)

M. Paraskeva, S.F. van Vuuren, S. Drewes and A.M. Viljoen, 2006. The antibacterial and anti-oxidant activity of South African indigenous *Commiphora* species and the isolated compounds from *C. glandulosa*. Podium presentation at the University of the Witwatersrand, International Conference on Pharmaceutical and Pharmacological Sciences (ICPPS). Vereeniging, Johannesburg, 20-23 September 2006 (Abstract in Appendix C)

## DEDICATION

---

I dedicate this dissertation to my parents,  
Panagiotis and Irene Paraskeva

Thank you for your valuable guidance, patience and understanding.

*“I have few illusions, but I feel a responsibility to work towards the things I consider good and right. I don’t know whether I will be able to change certain things for the better, or not at all. Both outcomes are possible. There is only one thing I will not concede and that is that it might be meaningless to strive in a good cause.”*

President Václav Havel of the Czech Republic

## ACKNOWLEDGEMENTS

---

This work was carried out at the University of the Witwatersrand, Johannesburg, Faculty of Health Sciences, Department of Pharmacy and Pharmacology, during the years 2005 and 2006.

Although I am the sole author of this dissertation, I am by no means the sole contributor. I would like to take this opportunity and use this as a platform to express my sincere gratitude to those who have contributed to my dissertation, to my education and to my life.

Firstly, to my supervisor Professor Alvaro Viljoen, for his constant enthusiasm and commitment, as well as his support at every brick wall that I encountered. Professor Viljoen has the enviable ability to always see the positive side to everything as well as to draw inspiration even in the deepest moments of disappointments and setbacks. Mostly I would like to offer gratitude to Prof. for allowing me to benefit from his wide knowledge in the field of Pharmacognosy, and for the steadfast encouragement to face all challenges and to embrace them. Thank you for giving me several enjoyable opportunities to present my research and providing just the right amount of guidance to ensure that my efforts contribute to the mainstream of Pharmaceutical chemistry.

I offer great thanks to my co-supervisor Mrs. Sandy van Vuuren, for her constant encouragement and kind attention. I would like to express my appreciation for all the support and guidance she offered, giving so generously of her time and expertise especially in the field of Microbiology. You, too, have been an inspiration, thank you!

I am grateful to Dr. Robyn van Zyl, who supervised the toxicity component of this dissertation, and I would also like to acknowledge Dr. Hajeera Davids for aiding immensely in the cancer work, your advice and assistance is much appreciated.

I am further indebted to Dr. Paul Steenkamp and Mr. Nial M. Harding for their technical guidance with the HPLC analysis.



## ACKNOWLEDGEMENTS *continued*

---

I would like to express my heartfelt gratitude to Professor Siegfried Drewes, Department of Chemistry, University of KwaZulu-Natal, for his collaboration and kind assistance in the final chemical characterisation of the two isolated compounds.

I am especially grateful to Mr. Marthinus Steyn for accompanying me on the field excursion which ensured the authenticity of all plant material collected.

I am also indebted to the National Research Foundation (Indigenous Knowledge Systems) for the financial assistance. I would also like to acknowledge the technical and administrative staff of the Department of Pharmacy and Pharmacology at the University of the Witwatersrand, for all their assistance.

Many thanks go to my friends and colleagues, Dr. Jeanette Lotter, Mr. Guy Kamatou, Miss Samantha Pillay, Miss Neha Singh, Miss Lisa du Toit, Miss Sheri-lee Harillal and Miss Ayesha Essop for sharing in the ups and downs of research, for the creative atmosphere that they brought forth in the laboratories and for their understanding and team spirit. A special thank you to Miss Miao-Juei Huang for being my audience the night before every conference presentation, and for her constant support and advice.

This dissertation emerged amid many friendships, providing lasting lessons, thank you to Miss Sanvila Puhça, Dr. Ana Rebic, Mr. Andrew Savvas, Mr. Paul Lambrou, Mr. George Christelis and Mrs. Voula Christelis.

In addition I would like to thank Miss Rupal Patel, whose belief in my abilities started me on this journey of my Masters degree. Thank you for your absolute confidence in me and for your constant encouragement and friendship throughout both my undergraduate and postgraduate degree.

## ACKNOWLEDGEMENTS *continued*

---

To a most remarkable friend, Miss Jacqueline Lalli. I feel an eternal gratitude for the friendship that we share. Thank you for brightening my days with your visits and outlooks and for putting up with me at my most stressful and sleep-deprived times. You never let me lose sight of my goals, and I appreciate your continued motivation and advice.

I am forever grateful to my grandparents, whose values encouraged the pursuit of a higher education. Thank you to the Argyrou, Dalakas, Fintanis and Terpizis families (in alphabetical order), and all other extended family, for providing unconditional love and support. I would like to thank my parents who provided me with the personal foundation and work ethic which has been so indispensable to both my personal and professional life. Your patience, understanding and love is much to be admired and appreciated. Knowing that you are always there to accommodate my erratic moods has always allowed me to be myself. Thank you for reminding me that though we are like mere threads of a tapestry, with no beginning and no end, tangled and in disarray, the way a tapestry looks from the back, the creator weaving the tapestry sees it from the front and knows the beauty of the picture He is creating.

To God, for always giving His fullest blessing.

The prayer of Jabez

*'Oh, that you would bless me indeed,  
and enlarge my territory,  
that Your hand would be with me,  
and that You would keep me from evil'*

# TABLE OF CONTENTS

---

---

<b>DECLARATION</b> .....	ii
<b>ABSTRACT</b> .....	iii
<b>PRESENTATIONS</b> .....	vi
<b>DEDICATION</b> .....	vii
<b>ACKNOWLEDGEMENTS</b> .....	viii
<b>TABLE OF CONTENTS</b> .....	xi
<b>LIST OF FIGURES</b> .....	xviii
<b>LIST OF TABLES</b> .....	xxv
<b>LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS</b> .....	xxix
<b>CHAPTER 1: GENERAL INTRODUCTION</b> .....	35
1.1 Ethnopharmacological research.....	37
1.2 An introduction to the family Burseraceae and genus <i>Commiphora</i> .....	37
1.2.1 The family: Burseraceae.....	37
1.2.2 The genus <i>Commiphora</i> .....	40
1.2.3 Characteristic features of <i>Commiphora</i> species.....	40
1.3 <i>Commiphora myrrha</i> .....	41
1.4 Medicinal uses of myrrh and guggul.....	43
1.4.1 <i>In vitro</i> pharmacological investigations of myrrh and guggul.....	44
1.4.2 <i>In vivo</i> pharmacological investigations of myrrh and guggul.....	45
1.4.3 Preclinical and clinical investigations of myrrh and guggul.....	47
1.5 The phytochemistry of myrrh.....	47
1.6 <i>Commiphora</i> and its traditional uses.....	47
1.6.1 <i>Commiphora</i> and its role in Ayurvedic medicine.....	50
1.6.2 <i>Commiphora</i> and its role in Chinese medicine.....	50
1.6.3 The African traditional uses of <i>Commiphora</i> species.....	51
1.6.4 Additional uses.....	51

1.7 A review of the phytochemistry documented for certain <i>Commiphora</i> species.....	52
1.8 Selection of plant material.....	52
1.8.1 The selection of <i>Commiphora</i> species for the screening of biological activities	55
1.8.2 The selection of biological activity assays performed.....	55
1.9 Aim of the study.....	56
1.10 Objectives of the study.....	56

## **CHAPTER 2: SPECIES STUDIED, PLANT COLLECTION**

### **AND PREPARATION OF THE EXTRACTS..... 59**

2.1 Brief introduction to the species under investigation.....	59
2.2 A description of the 10 indigenous <i>Commiphora</i> species under investigation.....	60
2.2.1 <i>Commiphora africana</i> (A.Rich.) Engl. var. <i>africana</i> .....	60
2.2.2 <i>Commiphora edulis</i> (Klotzsch) Engl. subsp. <i>edulis</i> .....	61
2.2.3 <i>Commiphora glandulosa</i> Schinz.....	62
2.2.4 <i>Commiphora marlothii</i> Engl.....	63
2.2.5 <i>Commiphora mollis</i> (Oliv.) Engl.....	64
2.2.6 <i>Commiphora neglecta</i> I.Verd.....	65
2.2.7 <i>Commiphora pyracanthoides</i> Engl.....	66
2.2.8 <i>Commiphora schimperi</i> (O.Berg) Engl.....	67
2.2.9 <i>Commiphora tenuipetiolata</i> Engl.....	68
2.2.10 <i>Commiphora viminea</i> Burt Davy.....	69
2.3 Preparation of plant extracts for determination of biological activity.....	70

## **CHAPTER 3: THE ANTI-OXIDANT ACTIVITY OF *COMMI-***

### ***PHORA* SPECIES AND THE ISOLATION OF KAEMPFEROL AND DIHYDROKAEMPFEROL..... 73**

3.1 Free radicals and their scavengers.....	73
3.1.1 Natural anti-oxidants.....	74
3.1.2 Flavonoids - their therapeutic potential.....	74

3.1.3	<i>Commiphora</i> and its anti-oxidant potential.....	75
3.1.4	Isolation of bio-active compounds.....	76
3.2	Materials and methods.....	78
3.2.1	Thin layer chromatography .....	78
3.2.2	2,2-diphenyl-1-picrylhydrazyl (DPPH) assay.....	79
3.2.2.1	Principle of the assay.....	79
3.2.2.2	Screening for anti-oxidant activity using thin layer chromatography .....	79
3.2.2.3	Colorimetric spectrophotometric assay.....	81
3.2.3	2,2'-Azino-bis(3-ethyl-benzthiazoline-6-sulfonic acid) (ABTS) assay.....	83
3.2.3.1	Principle of the assay.....	83
3.2.3.2	Screening for anti-oxidant activity using thin layer chromatography.....	83
3.2.3.3	Colorimetric spectrophotometric method.....	83
3.2.4	Isolation of compound 1 – column chromatography.....	85
3.2.4.1	Silica gel column chromatography .....	85
3.2.4.2	Size-exclusion column chromatography.....	86
3.2.5	Isolation of compound 2 – column chromatography.....	87
3.2.5.1	Silica gel column chromatography .....	87
3.2.5.2	Size-exclusion column chromatography.....	87
3.2.6	Nuclear magnetic resonance.....	87
3.2.7	Anti-oxidant activity of isolated compounds.....	89
3.3	Results.....	90
3.3.1	Screening for anti-oxidant activity using thin layer chromatography .....	90
3.3.2	Colorimetric spectrophotometric assays .....	91
3.3.3	Isolation of compounds .....	94
3.3.4	Isobologram construction of the interaction between the isolated compounds with anti-oxidant activity.....	98
3.4	Discussion.....	100
3.4.1	Screening for anti-oxidant activity using thin layer chromatography .....	100
3.4.2	Colorimetric spectrophotometric method.....	101
3.4.3	Isolation of compounds.....	108

3.4.4 Isobologram construction of the interaction between the isolated compounds with anti-oxidant activity.....	111
3.5 Conclusion .....	111
<b>CHAPTER 4: ANTIMICROBIAL ACTIVITY.....</b>	<b>113</b>
4.1 Introduction.....	113
4.1.1 Chemotherapeutic agents: factors affecting their effectiveness.....	113
4.1.2 Drug resistance.....	114
4.1.3 Natural products and their role in drug discovery.....	115
4.1.4 <i>Commiphora</i> species and their known antimicrobial activity.....	116
4.2 Materials and methods.....	116
4.2.1 Minimum inhibitory concentration assay.....	117
4.2.1.1 Principle of the method.....	117
4.2.1.2 Protocol.....	117
4.2.2 Death kinetic assay.....	119
4.2.2.1 Principle of the assay.....	119
4.2.2.2 Protocol.....	119
4.3 Results.....	122
4.3.1 Minimum inhibitory concentration.....	122
4.3.2 Death kinetic assay.....	123
4.4 Discussion.....	123
4.4.1 Minimum inhibitory concentration (MIC) assay.....	125
4.4.2 Death kinetic assay.....	131
4.5 Conclusion.....	131
<b>CHAPTER 5: ANTI-INFLAMMATORY ACTIVITY.....</b>	<b>134</b>
5.1 Introduction.....	134
5.1.1 Inflammatory response process.....	134
5.1.2 The lipxygenase system.....	134
5.1.3 The cyclo-oxygenase-1 and cyclo-oxygenase-2 enzyme system.....	138

5.1.4 <i>Commiphora</i> species and their anti-inflammatory effects.....	138
5.1.5 Flavonoids - their anti-inflammatory potential.....	140
5.2 Materials and methods.....	142
5.2.1 Principle of the assay.....	142
5.2.2 Protocol.....	142
5.2.2.1 Preparation of plant samples.....	142
5.2.2.2 5-Lipoxygenase assay.....	143
5.3 Results.....	144
5.4 Discussion.....	148
5.5 Conclusion.....	151
<b>CHAPTER 6: ANTICANCER ACTIVITY.....</b>	<b>152</b>
6.1 Introduction.....	152
6.1.1 Natural products and carcinogenesis defence.....	155
6.1.2 Flavonoids - a source of anticancer agents.....	156
6.1.3 The investigation of <i>Commiphora</i> as an anticancer agent.....	158
6.2 Materials and methods.....	162
6.2.1 Principle of the method.....	162
6.2.2 Protocol .....	162
6.2.2.1 Cell lines and cell culture.....	162
6.2.2.2 Preparation of plant samples.....	163
6.2.2.3 The sulforhodamine B assay.....	163
6.3 Results.....	166
6.4 Discussion.....	170
6.5 Conclusion.....	175

<b>CHAPTER 7: CYTOTOXICITY OF INDIGENOUS <i>COMMIPHORA</i> SPECIES</b> .....	177
7.1 Introduction.....	177
7.1.1 <i>Commiphora</i> and its cytotoxic properties.....	178
7.2 Materials and methods.....	179
7.2.1 Cytotoxicity.....	179
7.2.2 Principle of the method.....	180
7.2.3 Protocol.....	180
7.2.3.1 Cell culture maintenance.....	180
7.2.3.2 Preparation of plant samples.....	181
7.2.3.3 The 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) cellular viability assay .....	182
7.3 Results.....	183
7.4 Discussion.....	187
7.5 Conclusion.....	190
<b>CHAPTER 8: HIGH PERFORMANCE LIQUID CHROMATOGRAPHY</b> .....	191
8.1 Introduction .....	191
8.1.1 Flavonoids.....	192
8.1.2 Non-volatile chemical constituents found in <i>Commiphora</i> species.....	193
8.2 Materials and methods.....	194
8.3 Results.....	195
8.4 Discussion.....	203
8.5 Conclusion.....	209
<b>CHAPTER 9: GENERAL CONCLUSIONS</b> .....	211
<b>CHAPTER 10: RECOMMENDATIONS FOR FURTHER RESEARCH</b> .....	216



<b>REFERENCES</b> .....	219
<b>APPENDIX A - HPLC DATA</b> .....	249
<b>APPENDIX B – NMR DATA</b> .....	269
<b>APPENDIX C - ABSTRACTS OF PRESENTATIONS PRESENTED AT CONFERENCES</b> .....	273

## LIST OF FIGURES

---

<b>Figure 1.1:</b>	The tribal relationships within the family Burseraceae as revealed by the phylogeny of Clarkson <i>et al.</i> (2002).....	39
<b>Figure 1.2:</b>	The North American origin and dispersal hypothesis for Burseraceae. The map shows Eocene shorelines (53 Ma) and early Eocene fossil locations of Burseraceae (blue circles).....	39
<b>Figure 1.3:</b>	Characteristic features of <i>Commiphora</i> , with its papery bark, trifoliolate leaves, ripe fruit and pseudo-aril (left); pseudo-aril with exposed black seeded stone (right).....	41
<b>Figure 1.4:</b>	<i>Commiphora myrrh</i> , a thorny shrub, or small tree about 3m in height.....	42
<b>Figure 1.5:</b>	Oleo-gum-resin of myrrh.....	42
<b>Figure 1.6:</b>	A diagrammatic summary of indigenous <i>Commiphora</i> species, evaluating the phytochemistry and biological activities.....	58
<b>Figure 2.1:</b>	<i>Commiphora</i> species indigenous to South Africa (the species highlighted in bold were investigated in this study).....	59
<b>Figure 2.2:</b>	<i>Commiphora africana</i> leaves (left) and the recorded geographical distribution of the species (right).....	60
<b>Figure 2.3:</b>	<i>Commiphora edulis</i> tree with fruit (left) and the recorded geographical distribution of the species (right).....	61
<b>Figure 2.4:</b>	<i>Commiphora glandulosa</i> tree (left) and the recorded geographical distribution of the species (right).....	62
<b>Figure 2.5:</b>	<i>Commiphora marlothii</i> tree (left) and the recorded geographical distribution of the species (right).....	63
<b>Figure 2.6:</b>	<i>Commiphora mollis</i> tree (left) and the recorded geographical distribution of the species (right).....	64
<b>Figure 2.7:</b>	<i>Commiphora neglecta</i> tree bearing fruit (left) and the recorded geographical distribution of the species (right).....	65
<b>Figure 2.8:</b>	<i>Commiphora pyracanthoides</i> tree (left) and the recorded geographical distribution of the species (right).....	66

## LIST OF FIGURES *continued*

---

<b>Figure 2.9:</b>	<i>Commiphora schimperi</i> tree bearing fruit revealing pseudo-aril (left) and the recorded geographical distribution of the species (right).....	67
<b>Figure 2.10:</b>	<i>Commiphora tenuipetiolata</i> tree (left) with papery bark (insert) and the recorded geographical distribution of the species (right).....	68
<b>Figure 2.11:</b>	<i>Commiphora viminea</i> tree with characteristic bark that has dark horizontal bands (insert) and the recorded geographical distribution of the species (right).....	69
<b>Figure 3.1:</b>	Overview of procedure from extraction to identification.....	77
<b>Figure 3.2:</b>	Diagrammatic representation of chemical reaction of the reduction of DPPH in the presence of an electron donating anti-oxidant.....	80
<b>Figure 3.3:</b>	Representative 96-well microtiter plate, indicating final concentrations of plant extracts (left); A 96-well microtiter plate prepared for use in the DPPH assay. Purple wells indicate the absence of anti-oxidant effect, yellow wells are indicative of the presence of extracts with anti-oxidant activity (right).....	82
<b>Figure 3.4:</b>	Diagrammatic representation of the formation of the ABTS radical after the addition of potassium persulphate.....	84
<b>Figure 3.5:</b>	Glass column used in silica gel column chromatography for the isolation of compound 1. The extract was loaded onto the silica; the mobile phase was added at constant flow rates.....	86
<b>Figure 3.6:</b>	Schematic representation of the isolation and purification of compounds 1 (kaempferol) and 2 (dihydrokaempferol) isolated from <i>Commiphora glandulosa</i> (stem).....	88
<b>Figure 3.7:</b>	Isobologram depicting possible synergistic, antagonistic or additive effects as a result of either an interaction or a lack of interaction that exists between the compounds concerned.....	89

## LIST OF FIGURES *continued*

---

---

<b>Figure 3.8:</b>	Thin layer chromatography plate developed in a mobile phase consisting of toluene: dioxin: acetic acid (90:25:10), was used to determine the presence of anti-oxidant compounds present in the extracts of the <i>Commiphora</i> species studied, using the DPPH spray reagent. The anti-oxidant compounds are observed as yellow-white spots on a purple background.....	90
<b>Figure 3.9:</b>	Thin layer chromatography plate, developed in a mobile phase consisting of toluene: dioxin: acetic acid (90:25:10), indicating anti-oxidant compounds present in the extracts of the <i>Commiphora</i> species studied, using ABTS spray reagent.....	91
<b>Figure 3.10:</b>	Comparative DPPH and ABTS radical scavenging capacity of each of the <i>Commiphora</i> species extracts and the isolated kaempferol and Trolox control, demonstrated by IC <sub>50</sub> values with the exception of <i>C. edulis</i> leaves and <i>C. neglecta</i> leaves; the standard error of the mean of three replicates are denoted by error bars (n = 3 experiments).....	93
<b>Figure 3.11:</b>	The chemical structure of kaempferol (compound 1).....	95
<b>Figure 3.12:</b>	The chemical structure of dihydrokaempferol (compound 2).....	96
<b>Figure 3.13:</b>	Isobologram of the interaction between <i>Commiphora glandulosa</i> (stem) and vitamin C, showing a synergistic relationship.....	99
<b>Figure 3.14:</b>	Isobologram of the interaction between isolated compounds kaempferol and dihydrokaempferol, showing an antagonistic relationship.....	100
<b>Figure 3.15:</b>	The mechanism of DPPH radical scavenging by kaempferol as proposed by Tsimogiannis and Oreopoulou (2006).....	104
<b>Figure 3.16:</b>	The basic chemical structure of flavonols.....	106
<b>Figure 3.17:</b>	Isolated steps from the metabolic pathway of flavonoids.....	110

## LIST OF FIGURES *continued*

---

<b>Figure 4.1:</b>	Representative 96-well microtiter plate, indicating final concentrations of plant extracts (left); A 96-well microtiter plate prepared for use in the MIC assay. Red wells indicate the absence of inhibitory activity (or the presence of <i>p</i> -iodonitrotetrazolium) (right).....	120
<b>Figure 4.2:</b>	Log <sub>10</sub> reduction time kill plot of <i>Commiphora marlothii</i> .....	123
<b>Figure 4.3:</b>	The comparative structural complexity of the outer membranes and cell walls of Gram- negative and Gram- positive bacteria.....	126
<b>Figure 5.1:</b>	The translocation of 5-lipoxygenase and cytosolic phospholipase A <sub>2</sub> , upon cellular stimulation, to the nuclear membrane, followed by the substantial generation of leukotrienes.....	135
<b>Figure 5.2:</b>	Schematic representation of the 5-lipoxygenase pathway and simplified scheme of the generation of other eicosanoids from arachidonic acid, indicating the cyclo-oxygenase pathway.....	137
<b>Figure 5.3:</b>	The basic chemical structure of flavones.....	140
<b>Figure 5.4:</b>	The chemical structure of a prenylated flavonoid, kuwanon C.....	141
<b>Figure 5.5:</b>	Schematic representation of the 5-lipoxygenase assay.....	144
<b>Figure 5.6:</b>	The percentage 5-lipoxygenase enzyme inhibition by <i>Commiphora</i> leaf and stem extracts at a concentration of 100 µg/ml.....	147
<b>Figure 6.1:</b>	Flavonoids that block or suppress multi-stage carcinogenesis.....	157
<b>Figure 6.2:</b>	The chemical structures of podophyllotoxin, 4-deoxypodophyllotoxin and Erlangerin A - D.....	159
<b>Figure 6.3:</b>	The chemical structure of guggulsterone.....	160
<b>Figure 6.4:</b>	Molecular targets of dietary agents for the prevention and therapy of cancers. Highlighted in orange are the targets of guggulsterone isolated from <i>Commiphora mukul</i> .....	161

## LIST OF FIGURES *continued*

---

<b>Figure 6.5:</b>	Representative 96-well microtiter plate, indicating concentrations of plant extracts (left); A 96-well microtiter plate prepared for use in the SRB assay. Pink wells are an indication of stained cells (right).....	165
<b>Figure 6.6:</b>	Percentage cell growth inhibition of <i>Commiphora neglecta</i> (leaf) against the MCF-7 cell line, <i>C. viminea</i> (leaf) against the HT-29 cell line and <i>C. edulis</i> (leaf) against the SF-268 cell line, indicating the concentration-dependent inhibitory effect.....	168
<b>Figure 6.7:</b>	Representative antiproliferative activity at 100 µg/ml of indigenous <i>Commiphora</i> species under investigation and 5'-Fluorouracil in the SRB assay against two cancer cell lines - the neuronal SF-268 and colon adenocarcinoma HT-29 cell lines; the standard error of the mean of three replicates are denoted by error bars (n = 3 experiments).....	169
<b>Figure 6.8:</b>	The basic chemical structure of flavones.....	172
<b>Figure 7.1:</b>	Representative 96-well microtiter plate indicating final concentrations of plant extracts and arrangement of controls prepared for use in the MTT assay.....	181
<b>Figure 7.2:</b>	The IC <sub>50</sub> values depicting the cytotoxicity of the 10 stems and leaves of indigenous <i>Commiphora</i> species, ; the standard error of the mean of three replicates are denoted by error bars (n = 3 experiments).....	185
<b>Figure 7.3:</b>	A comparison between the cytotoxicity elicited by <i>Commiphora</i> species on the normal human transformed kidney epithelium cells in the MTT assay and the breast adenocarcinoma MCF-7 cell line in the SRB assay...	186
<b>Figure 8.1:</b>	The basic chemical structure of flavonoids.....	193
<b>Figure 8.2:</b>	HPLC chromatograms of 10 indigenous <i>Commiphora</i> stem extracts.....	196
<b>Figure 8.3:</b>	HPLC chromatograms of 10 indigenous <i>Commiphora</i> leaf extracts.....	197
<b>Figure 8.4:</b>	The chemical structures and corresponding UV spectra of a flavonol (left) and a flavone (right).....	199

## LIST OF FIGURES *continued*

---

<b>Figure 8.5:</b>	The chemical structure, corresponding UV spectrum (insert), and HPLC chromatogram of kaempferol.....	202
<b>Figure 8.6:</b>	Chromatogram of <i>Commiphora pyracanthoides</i> (stem) with UV absorption maxima (insert) of compounds eluting at the retention times 13.73 min and 14.72 min.....	206
<b>Figure 8.7:</b>	Chromatogram of <i>Commiphora edulis</i> (stem, top) and <i>Commiphora edulis</i> (leaves, bottom), with UV absorption maxima of compounds eluting at the retention times of approximately 34.02 min and 34.50 min.....	207
<b>APPENDIX A</b>		
<b>Figure A1:</b>	HPLC chromatogram of <i>Commiphora africana</i> stem extract.....	249
<b>Figure A2:</b>	HPLC chromatogram of <i>Commiphora africana</i> leaf extract.....	250
<b>Figure A3:</b>	HPLC chromatogram of <i>Commiphora edulis</i> stem extract.....	251
<b>Figure A4:</b>	HPLC chromatogram of <i>Commiphora edulis</i> leaf extract.....	252
<b>Figure A5:</b>	HPLC chromatogram of <i>Commiphora glandulosa</i> stem extract.....	253
<b>Figure A6:</b>	HPLC chromatogram of <i>Commiphora glandulosa</i> leaf extract.....	254
<b>Figure A7:</b>	HPLC chromatogram of <i>Commiphora marlothii</i> stem extract.....	255
<b>Figure A8:</b>	HPLC chromatogram of <i>Commiphora marlothii</i> leaf extract.....	256
<b>Figure A9:</b>	HPLC chromatogram of <i>Commiphora mollis</i> stem extract.....	257
<b>Figure A10:</b>	HPLC chromatogram of <i>Commiphora mollis</i> leaf extract.....	258
<b>Figure A11:</b>	HPLC chromatogram of <i>Commiphora neglecta</i> stem extract.....	259
<b>Figure A12:</b>	HPLC chromatogram of <i>Commiphora neglecta</i> leaf extract.....	260
<b>Figure A13:</b>	HPLC chromatogram of <i>Commiphora pyracanthoides</i> stem extract.....	261
<b>Figure A14:</b>	HPLC chromatogram of <i>Commiphora pyracanthoides</i> leaf extract.....	262
<b>Figure A15:</b>	HPLC chromatogram of <i>Commiphora schimperi</i> stem extract.....	263
<b>Figure A16:</b>	HPLC chromatogram of <i>Commiphora schimperi</i> leaf extract.....	264

## LIST OF FIGURES *continued*

---

<b>Figure A17:</b>	HPLC chromatogram of <i>Commiphora tenuipetiolata</i> stem extract.....	265
<b>Figure A18:</b>	HPLC chromatogram of <i>Commiphora tenuipetiolata</i> leaf extract.....	266
<b>Figure A19:</b>	HPLC chromatogram of <i>Commiphora viminea</i> stem extract.....	267
<b>Figure A20:</b>	HPLC chromatogram of <i>Commiphora viminea</i> leaf extract.....	268
<b>APPENDIX B</b>		
<b>Figure B1</b>	$^1\text{H}$ NMR spectrum of Compound <b>1</b> .....	269
<b>Figure B2</b>	$^{13}\text{C}$ NMR spectrum of Compound <b>1</b> .....	270
<b>Figure B3</b>	$^1\text{H}$ NMR spectrum of Compound <b>2</b> .....	271
<b>Figure B4</b>	$^{13}\text{C}$ NMR spectrum of Compound <b>2</b> .....	272



## LIST OF TABLES

---

---

<b>Table 1.1:</b>	Drugs derived from plants, their clinical uses and sources.....	36
<b>Table 1.2:</b>	The different sources of myrrh and their chemical constituents.....	48
<b>Table 1.3:</b>	The traditional uses of <i>Commiphora</i> species indigenous to southern Africa.....	51
<b>Table 1.4:</b>	The phytoconstituents of extracts and the oleo-gum-resin documented for a few species of <i>Commiphora</i> ... presenting interesting chemical profiles, adapted from Hanuš <i>et al.</i> (2005).....	53
<b>Table 2.1:</b>	Collection data for the 10 indigenous <i>Commiphora</i> species under investigation.....	72
<b>Table 3.1:</b>	<i>In vitro</i> anti-oxidant activity ( $\mu\text{g/ml}$ ) of extracts from indigenous <i>Commiphora</i> species, as shown by the DPPH and ABTS assays. Results are given as mean $\pm$ s.d, n=3.....	92
<b>Table 3.2:</b>	Comparing the experimental data of $^1\text{H}$ NMR of the aglycone kaempferol with that obtained by Bin and Yongmin (2003), Soliman <i>et al.</i> (2002) and Xu <i>et al.</i> (2005).....	95
<b>Table 3.3:</b>	Comparing the experimental data of $^{13}\text{C}$ NMR of the aglycone kaempferol with that obtained by Bin and Yongmin (2003), Soliman <i>et al.</i> (2002) and Xu <i>et al.</i> (2005).....	96
<b>Table 3.4:</b>	Comparing the experimental data of $^1\text{H}$ NMR of dihydrokaempferol with that obtained by Güvenalp and Demirezer (2005) and Xu <i>et al.</i> (2005).....	97
<b>Table 3.5:</b>	Comparing the experimental data of $^{13}\text{C}$ NMR of dihydrokaempferol with that obtained by Güvenalp and Demirezer (2005) and Xu <i>et al.</i> (2005).....	97
<b>Table 3.6:</b>	Data generated for the construction of the isobologram to indicate the interaction between <i>Commiphora glandulosa</i> stem extract and vitamin C, in the DPPH assay.....	98
<b>Table 3.7:</b>	Data generated for the construction of the isobologram to indicate the interaction between kaempferol and dihydrokaempferol, in the DPPH assay.....	99

## LIST OF TABLES *continued*

---

<b>Table 4.1:</b>	MIC values obtained for extracts of indigenous <i>Commiphora</i> species against <i>Staphylococcus aureus</i> , <i>Bacillus cereus</i> , <i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Candida albicans</i> , <i>Cryptococcus neoformans</i> . n = 3.....	124
<b>Table 5.1:</b>	The percentage 5-lipoxygenase enzyme inhibitory activity of <i>Commiphora</i> species stem and leaf extracts <i>in vitro</i> at 100 µg/ml and their corresponding IC <sub>50</sub> values.....	145
<b>Table 6.1:</b>	Incidence rates of the major cancers in the caucasian and black population of South Africa.....	153
<b>Table 6.2:</b>	Cytotoxic drugs developed from plant sources.....	154
<b>Table 6.3:</b>	The percentage cell growth inhibition (CGI) of colon adenocarcinoma cell line (HT-29), breast adenocarcinoma cell line (MCF-7) and neuronal cell line (SF-268) on exposure to stem and leaf extracts of indigenous <i>Commiphora</i> species, kaempferol and reference compound 5'-Fluorouracil, and the IC <sub>50</sub> values of the respective species. Results are given as mean ± s.d, n=3 .....	167
<b>Table 7.1:</b>	The cytotoxicity of extracts of indigenous <i>Commiphora</i> species, kaempferol and quinine against the transformed human kidney epithelium cells. Results are given as mean ± s.d, n=3.....	184
<b>Table 8.1:</b>	HPLC-UV maxima of the tentatively identified flavonoid derivatives present in the <i>Commiphora</i> leaf extracts.....	198
<b>Table 8.2:</b>	HPLC results of the compounds, expressed in percentage area, detected in <i>Commiphora</i> stem extracts.....	200
<b>APPENDIX</b>		
<b>Table A1:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora africana</i> stem extract.....	249
<b>Table A2:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora africana</i> leaf extract.....	250

## LIST OF TABLES *continued*

---

---

<b>Table A3:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora edulis</i> stem extract.....	xxvii
<b>Table A4:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora edulis</i> leaf extract.....	252
<b>Table A5:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora glandulosa</i> stem extract.....	253
<b>Table A6:</b>	Retention time, percentage integration area, and UV maxima for peaks from <i>Commiphora glandulosa</i> leaf extract.....	254
<b>Table A7:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora marlothii</i> stem extract.....	255
<b>Table A8:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora marlothii</i> leaf extract.....	256
<b>Table A9:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora mollis</i> stem extract.....	257
<b>Table A10:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora mollis</i> leaf extract.....	258
<b>Table A11:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora neglecta</i> stem extract.....	259
<b>Table A12:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora neglecta</i> leaf extract.....	260
<b>Table A13:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora pyracanthoides</i> stem extract.....	261
<b>Table A14:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora pyracanthoides</i> leaf extract.....	262
<b>Table A15:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora schimperi</i> stem extract.....	263
<b>Table A16:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora schimperi</i> leaf extract.....	264

## LIST OF TABLES *continued*

---

---

<b>Table A17:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora tenuipetiolata</i> stem extract.....	265
<b>Table A18:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora tenuipetiolata</i> leaf extract.....	266
<b>Table A19:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora viminea</i> stem extract.....	267
<b>Table A20:</b>	Retention time, percentage integration area and UV maxima for peaks from <i>Commiphora viminea</i> leaf extract.....	268

## LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS

---

<b>ABTS:</b>	2,2'-azino-bis(3-ethyl-benzthiazoline-6-sulfonic acid)
<b>AKT:</b>	Activated protein kinase
<b>AP-1:</b>	Activator protein 1
<b>ATCC:</b>	American Type Culture Collection (Manassas, VA, USA)
<b>ATP:</b>	Adenosine Triphosphate
<b>AR:</b>	Androgen Receptor
<b>AV:</b>	Voucher specimen numbers (Alvaro Viljoen)
<b>Av:</b>	Average
<b>Bax:</b>	Bcl2-associated X protein
<b>Bcl2:</b>	B-cell lymphoma-2
<b>C<sub>2</sub>:</b>	Carbon 2
<b>C<sub>3</sub>:</b>	Carbon 3
<b>C<sub>6</sub>:</b>	Carbon 6
<b>ca.:</b>	Circa (around; about)
<b>CAL:</b>	<i>Commiphora africana</i> leaves
<b>CAS:</b>	<i>Commiphora africana</i> stem
<b>Cdk:</b>	Cyclin-dependent kinase
<b>CEL:</b>	<i>Commiphora edulis</i> leaves
<b>CES:</b>	<i>Commiphora edulis</i> stem
<b>cFLIP:</b>	Cellular FADD-like interleukin-1-converting enzyme (FLICE) inhibitory protein
<b>CFU:</b>	Colony forming units
<b>CGL:</b>	<i>Commiphora glandulosa</i> leaves
<b>CGS:</b>	<i>Commiphora glandulosa</i> stem
<b>clAP:</b>	Cellular inhibitor of apoptosis protein
<b>CM<sub>A</sub>L:</b>	<i>Commiphora marlothii</i> leaves
<b>CM<sub>A</sub>S:</b>	<i>Commiphora marlothii</i> stem
<b>CML:</b>	<i>Commiphora mollis</i> leaves
<b>CMS:</b>	<i>Commiphora mollis</i> stem
<b>CNL:</b>	<i>Commiphora neglecta</i> leaves
<b>CNS:</b>	<i>Commiphora neglecta</i> stem

## LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS *continued*

---

<b>CO<sub>2</sub>:</b>	Carbon dioxide
<b>CPL:</b>	<i>Commiphora pyracanthoides</i> leaves
<b>CPS:</b>	<i>Commiphora pyracanthoides</i> stem
<b>CSF:</b>	Colony stimulating factors
<b>CSL:</b>	<i>Commiphora schimperi</i> leaves
<b>CSS:</b>	<i>Commiphora schimperi</i> stem
<b>CTL:</b>	<i>Commiphora tenuipetiolata</i> leaves
<b>CTS:</b>	<i>Commiphora tenuipetiolata</i> stem
<b>CVL:</b>	<i>Commiphora viminea</i> leaves
<b>CVS:</b>	<i>Commiphora viminea</i> stem
<b>COX:</b>	Cyclo-oxygenase
<b>°C:</b>	Degrees Celsius
<b>DMEM:</b>	Dulbecco's Modified Eagle's Medium
<b>DMSO:</b>	Dimethyl sulfoxide
<b>DNA:</b>	Deoxyribonucleic acid
<b>DPPH:</b>	2,2-diphenyl-1-picrylhydrazyl
<b>DSM:</b>	Deutsche Sammlung von Mikroorganismen (culture collection; Braunschweig, Germany)
<b>EDTA:</b>	Ethylene diamine tetraacetic acid
<b>EGF:</b>	Epidermal growth factor
<b>EGFR:</b>	Epidermal growth factor receptor
<b>Egr-1:</b>	Early growth response 1
<b>ELAM:</b>	Endothelial leucocyte adhesion molecule
<b>EpRE:</b>	Electrophile responsive element
<b>ER-<math>\alpha</math>:</b>	Estrogen receptor alpha
<b>ER-<math>\beta</math>:</b>	Estrogen receptor beta
<b>FCS:</b>	Foetal calf serum
<b>FGF:</b>	Fibroblast growth factor
<b>FLAP:</b>	5-Lipoxygenase activating protein
<b>FTPase:</b>	Farnesyl-protein transferase
<b>FXR:</b>	Farnesoid X receptor
<b>g:</b>	Gram

## LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS *continued*

---

<b>GC:</b>	Gas chromatography
<b>GPS:</b>	Global positioning system
<b>GST:</b>	Glutathione S-transferase
<b>GST-px:</b>	Glutathione peroxidase
<b>HER2:</b>	Human epidermal growth factor receptor 2
<b>HETE:</b>	Hydroxyeicosatetraenoic acid
<b>HL-60:</b>	Leukemic cancer cell line
<b>5-HPETE:</b>	5-hydroxyperoxyeicosatetraenoic acid
<b>HPLC:</b>	High performance liquid chromatography
<b>HPLC-UV:</b>	High performance liquid chromatography-ultraviolet
<b>HPRT:</b>	Hypoxanthine guanine phosphoribosyl transferase
<b>HT-29:</b>	Colon adenocarcinoma cell line
<b>H<sub>2</sub>O<sub>2</sub>:</b>	Di-hydrogen Dioxide (Hydrogen peroxide)
<b>OH:</b>	Hydroxide
<b>ICAM-1:</b>	Intercellular adhesion molecule-1
<b>IC<sub>50</sub>:</b>	Inhibitory concentration
<b>IFN-<math>\gamma</math>:</b>	Interferon gamma
<b>IGF:</b>	Insulin-like growth factor
<b>IKK:</b>	IkappaBalph kinase
<b>IL-1:</b>	Interleukin
<b>iNOS:</b>	Inducible nitric oxide synthase
<b>INT:</b>	<i>p</i> -iodonitrotetrazolium
<b>JAK2:</b>	Janus kinase 2 protein kinase
<b>JNK:</b>	c Jun N-terminal kinase
<b>KH<sub>2</sub>PO<sub>4</sub>:</b>	Potassium di-hydrogenphosphate
<b>K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>:</b>	Potassium persulfate
<b><math>\lambda</math>:</b>	Lambda (wavelength)
<b>LOX:</b>	Lipoxygenase
<b>LPS:</b>	Lipopolysaccharide
<b>m:</b>	Meters
<b>Ma:</b>	Million years ago

## LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS *continued*

---

<b>MAPK:</b>	Mitogen-activated protein kinases
<b>MCF-7:</b>	Breast adenocarcinoma cell line
<b>MDR:</b>	Multiple drug resistance
<b>mg:</b>	Milligram
<b>MIC:</b>	Minimum inhibitory concentration
<b>min:</b>	Minutes
<b>ml:</b>	Milliliter
<b>mM:</b>	Millimolar
<b>MMP:</b>	Matrix metalloproteinase
<b>MTT:</b>	3-[4,5-Dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide
<b>µg:</b>	Microgram
<b>µl:</b>	Microlitre
<b>n:</b>	Number of experimental runs
<b>NaCl:</b>	Sodium chloride
<b>NADH:</b>	Nicotinamide adenine dinucleotide
<b>NADPH:</b>	Nicotinamide adenine dinucleotide phosphate
<b>NaHCO<sub>3</sub>:</b>	Sodium hydrogen carbonate
<b>Na<sub>2</sub>HPO<sub>4</sub>·2 H<sub>2</sub>O:</b>	Di-sodium hydrogenphosphate dehydrate
<b>NCI:</b>	National cancer institute
<b>NCTC:</b>	National collection of type cultures (Central Public Laboratory Service, London, UK)
<b>NDGA:</b>	Nordihydroguaiaretic acid
<b>NF-κB:</b>	Nuclear factor-kappa B
<b>nm:</b>	Nanometer
<b>NMR:</b>	Nuclear magnetic resonance
<b>NR:</b>	Nuclear receptors
<b>Nrf2:</b>	NF-E2-related Factor 2
<b>NSAID:</b>	Non-steroidal anti-inflammatory drugs
<b>NW:</b>	New world
<b>OW:</b>	Old world
<b>O<sub>2</sub>:</b>	Oxygen



## **LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS *continued***

---

<b>PARP:</b>	Polyadenosine-5'-diphosphate-ribose polymerase
<b>PBS:</b>	Phosphate buffer saline
<b>PCA:</b>	Principle component analysis
<b>PDGF:</b>	Platelet-derived growth factor
<b>Pgp:</b>	P-glycoprotein
<b>pH:</b>	Potential hydrogen
<b>PKA:</b>	Protein kinase A
<b>PKC:</b>	Protein kinase C
<b>PLA<sub>2</sub>:</b>	Phospholipase A <sub>2</sub>
<b>PPAR<math>\gamma</math>:</b>	Peroxisome proliferator-activated receptor gamma
<b>ppm:</b>	Parts per million
<b>p21/WAF:</b>	Cyclin dependent kinase inhibitor complex
<b>p27Kip/Cip:</b>	Cyclin dependent kinase inhibitor complex
<b>p53:</b>	Tumour suppressor gene
<b>R<sub>f</sub>:</b>	Retention factor
<b>RNA:</b>	Ribonucleic Acid
<b>ROS:</b>	Reactive oxygen species
<b>rpm:</b>	Revolutions per minute
<b>RPMI 1640:</b>	Roswell Park Memorial Institute Media 1640
<b>s:</b>	Seconds
<b>SABS:</b>	South African Bureau for Standards
<b>SAR:</b>	Structure-activity relationship
<b>s.d.:</b>	Standard deviation
<b>SDG:</b>	Succinate-dehydrogenase
<b>SF-268:</b>	Neuronal glioblastoma cancer cell line
<b>spp.:</b>	Species
<b>SRB:</b>	Sulphorhodamine
<b>Src:</b>	protein kinase
<b>STAT:</b>	Signal transducer and activator of transcription
<b>subsp.:</b>	Subspecies
<b>syn.:</b>	Synonym

## LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS *continued*

<b>TEAC:</b>	Trolox equivalent anti-oxidant capacity
<b>TGF<math>\alpha</math>/<math>\beta</math>:</b>	Transforming growth factor alpha/beta
<b>TLC:</b>	Thin layer chromatography
<b>TNF:</b>	Tumour necrosis factor
<b>TRAF1:</b>	Tumour necrosis factor receptor-associated factor
<b>TSA:</b>	Tryptone soya agar
<b>TSB:</b>	Tryptone soya broth
<b>TYK2:</b>	Tyrosine kinase 2
<b>uPA:</b>	Urokinase-type plasminogen activator
<b>UV:</b>	Ultra violet
<b>UV-VIS:</b>	Ultraviolet-visible
<b>var:</b>	Variant
<b>VCAM:</b>	Vascular cell adhesion molecule
<b>VEGF:</b>	Vascular endothelial growth factor
<b>vs:</b>	Versus
<b>WHO:</b>	World Health Organization
<b>w/v:</b>	Weight per volume
<b>xIAP:</b>	Inhibitor of apoptosis protein
<b>↓:</b>	Decrease
<b>↑:</b>	Increase