

***The Synthesis and Antioxidant Capacities of a
range of Resveratrol and Related Phenolic
Glucosides.***

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requirements for the degree of*

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Abstract

The resveratrol analogues have attracted great attention by scientists as these compounds exhibit numerous bioactive properties due to their outstanding antioxidant capacity. However, the role of the antioxidant activity of these molecules is still not quite clear. This thesis details the development and biological evaluation of a library of resveratrol analogues in order to provide a better understanding of their pharmaceutical value.

This thesis begins with an overview of an important hydroxylated stilbene (resveratrol) and its analogues present in natural plants, food and beverage. Consequently, these studies are summarised and aided in the selection of a new library of substrates to be synthesised herein and biologically evaluated.

Chapter two details the successful synthesis of resveratrol glycosides from resveratrol. Pleasingly, all chemical transformations carried out herein were performed in excellent yields. *In-vitro* anti-oxidant studies on these substrates revealed glycosylation of resveratrol leads to a decreased antioxidant capacity. In addition, these studies suggested the para hydroxyl group on resveratrol has a higher reactivity than the meta hydroxyl group.

Chapter three details the synthesis of a hydroxylated resveratrol (piceatannol) and many of its glycosides. Almost all of the targeted compounds were prepared by applying a modified strategy designed for resveratrol glycosides in high efficiency. The anti-oxidant assays suggested that piceatannol is a more powerful antioxidant than resveratrol. The assays also revealed that the antioxidant activity of piceatannol glycosides is quite dependent on the glycosylation position.

Chapter four then details the preparation of several common resveratrol dimers. The individual products were obtained via a one step oxidation of resveratrol followed by acetylation of the products, separation, and base hydrolysis. In addition, successful isomerisation of some of the *trans*-dimers into their *cis* forms was achieved in this study. With a simple protocol now in place to synthesise such resveratrol dimers, it paves the way for future work on the synthesis of glucosylated dimers of resveratrol. Such compounds would be expected to have a diverse range of antioxidant properties and other related bioactivities and are worthy of further exploration.

Finally, Chapter five contains the associated experimental procedures and characterisation data for all synthesised resveratrol and piceatannol analogues along with a range of oligomers.

List of publications

1. Fragmentation Patterns of Monomeric and Oligomeric Wine Stilbenoids by UHPLC-ESI-QTOFMS. Moss, R.; Mao, Q.; Taylor, D.; Saucier, C. *Rapid Communications in Mass Spectrometry*, **2013**, 27, 1815-1827.
2. Pallidol hexaacetate ethyl acetate monosolvate. Mao, Q.; Taylor, D. K.; Ng, S. W.; Tiekink, E. R. T. *Acta Crystallographica Section E*, **2013**, E69, 1155-1156.
3. Synthesis and Antioxidant Capacity Studies of Resveratrol of all Possible Glucosides. Mao, Q.; Skouroumounis, G.; Taylor, D. K. *Natural Products*. **2015**, *In Preparation*.
4. Synthesis and Antioxidant Capacity Studies of Piceatannol Glucosides. Mao, Q.; Skouroumounis, G.; Taylor, D. K. *Natural Products*. **2015**, *In Preparation*.

Declaration

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Q Mao

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Abbreviations

ABS	Absorbance
br	Broad
COSY	Correlation spectroscopy
cm	Centimetres
d	Doublet
DCM	Dichloromethane
DMSO	Dimethyl sulfoxide
dd	Doublet of doublets
ddd	Doublet of doublet of doublets
DPPH	2,2-Diphenyl-1-picrylhydrazyl-1,1-diphenyl-2-picrylhydrazyl
Et	Ethyl
Et ₂ O	Diethyl ether
EtOAc	Ethyl acetate
EtOH	Ethanol
FeCl ₃	Ferric chloride
FRAP	Ferric cyanide reducing antioxidant power assay
g	Grams
GC	Gas chromatography
GCMS	Gas chromatography mass spectrometry
h	Hours
HCl	Hydrochloric acid
HMBC	Heteronuclear multiple bond correlation
HMQC	Heteronuclear multiple quantum coherence
HPLC-DAD	High-Performance Liquid Chromatography-Diode-Array Detection
HRMS	High resolution mass spectrometry
Hz	Hertz
$h\nu$	Light/irradiation
J	Coupling constant
K ₂ CO ₃	Potassium carbonate
L	Litre
LC-MS	Liquid chromatography-mass spectrometry
Lit.	Literature

m	Multiplet
M	Molar (moles/litre)
min.	Minutes
m/z	Mass to charge ratio
MeOH	Methanol
MgSO ₄	Magnesium sulphate
mg	Milligrams
MHz	Megahertz
mL	Millilitre
mmol	Millimoles
mol	Moles
Mpt.	Melting point
MS	Mass spectrometry
nm	Nanometres
Na	Sodium
NaHCO ₃	Sodium bicarbonate
NMR	Nuclear magnetic resonance
OAc	Acetate
Piv	Pivaloyl
ppm	Parts per million
psi	Pounds per square inch
q	Quartet
R _f	Retention factor
rt	Room temperature
s	Singlet
t	Triplet
TBS	<i>tert</i> -Butyldimethylsilyl
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TPTZ	2,4,6-Tripyridyl-1,3,5-triazin
UV	Ultra-violet
<i>d</i>	Chemical shift
<i>m</i>	Micro

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*“God in his goodness sent the grapes, to cheer both great and small; little
fools drink too much, and great fools not at all.”*

-Anonymous

*‘Wine is a biochemical challenge. It is a daunting task
to probe the alchemy of this elixir and to determine
what lies ‘at the heart of the matter’.’*

-Goldberg