

**GREEN APPROACH TO SYNTHESIS
OF OXINDOLE DERIVATIVES AND
INVESTIGATION OF THEIR
ANTIMICROBIAL AND
ANTIOXIDANT ACTIVITIES**

By

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WIJEKON**

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Thesis submitted to the University of Sri Jayewardenepura for the
award of the Degree of Master of Philosophy

DECLARATION BY THE CANDIDATE

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TABLE OF CONTENTS

TABLE OF CONTENTS	i
LIST OF TABLES	vii
LIST OF FIGURES	viii
LIST OF SCHEMES	xiv
LIST OF ABBREVIATIONS	xv
ACKNOWLEDGEMENT	xvii
ABSTRACT	xviii
INTRODUCTION	1
1.1 Overview	1
1.2 Objectives of the study	4
LITERATURE REVIEW	5
2.1 Introduction to Oxindole	5
2.2 Pharmaceutical important Oxindole derivatives	6
2.3 3-Alkenyl oxindole derivatives	7
2.3.1 Naturally occurring 3-Alkenyl oxindole derivatives.....	8
2.3.2 3-Alkenyl oxindole derivatives with pharmaceutical importance	9
2.3.3 3-Alkenyl oxindole derivatives as antimicrobial agents	11
2.3.4 Methods used in the detection of antimicrobial activity	13
2.3.4.1 Agar well diffusion assay	13
2.3.4.2 Resazurin assay.....	13
2.3.5 3-Alkenyl oxindole derivatives as antioxidants	13
2.3.6 Methods used in the detection of antioxidant activity	14

2.3.7	Cytotoxicity of 3-Alkenyl oxindole derivatives.....	15
2.3.8	Brine shrimp lethality assay in the detection of cytotoxicity.....	16
2.4	Synthesis of 3-Alkenyl oxindole derivatives.....	16
2.5	Microwave-Assisted Organic Synthesis (MAOS).....	18
2.5.1	Applications of microwave in organic synthesis	18
2.5.2	Solid supported MAOS.....	21
2.5.3	Silica as a solid support in organic synthesis.....	22
2.5.4	Preparation of silica from rice husk.....	24
2.5.5	Silane reagents as linkers	25
2.5.6	APTES functionalized silica as a catalyst.....	26
2.5.7	H ₂ SO ₄ Functionalized silica as a catalyst.....	27
MATERIALS AND METHODS		29
3.1	Materials and instrumentation.....	30
3.1.1	Chemicals.....	30
3.1.2	Solvents.....	30
3.1.3	Analytical Instruments	31
3.1.4	Apparatus and Equipment.....	31
3.1.5	Culture of microorganisms and microbial culture media.....	31
3.1.6	Modification of domestic microwave oven.....	32
3.2	Preparation of APTES-Silica.....	33
3.2.1	Extraction of silica from rice husk.....	33
3.2.2	Activation of rice husk silica.....	33
3.2.3	Preparation of APTES functionalized silica	34
3.2.4	Characterization of APTES-Silica	35

3.2.4.1	Fourier Transform Infrared spectroscopy (FTIR).....	35
3.2.4.2	Powder X-ray diffraction (XRD).....	35
3.2.4.3	Thermogravimetric analysis (TGA)	35
3.2.4.4	Scanning Electron Microscopic (SEM) Analysis	35
3.2.4.5	Elemental Analysis	35
3.3	Microwave-assisted solvent free synthesis of 3-Alkenyl oxindole derivatives	36
3.3.1	Optimization of the reaction conditions.....	36
3.3.2	Synthesis of 3-Alkenyl oxindole derivatives	37
3.3.3	Reaction monitoring by Thin Layer Chromatography (TLC).....	39
3.3.4	Reusability of APTES-Silica.....	40
3.3.5	Characterization of 3-Alkenyl oxindole derivatives	40
3.3.5.1	Determination of melting point	40
3.3.5.2	Nuclear Magnetic Resonance (NMR) Analysis	40
3.3.5.3	FTIR.....	40
3.3.5.4	Ultraviolet-Visible spectroscopy (UV-Vis) Analysis.....	41
3.4	H ₂ SO ₄ -Silica	41
3.4.1	Synthesis of H ₂ SO ₄ -Silica	41
3.4.2	Characterization of H ₂ SO ₄ -Silica.....	41
3.5	Microwave assisted solvent-free synthesis of <i>N</i> -acetylated-3-alkenyl oxindoles	41
3.5.1	Thin Layer Chromatography (TLC).....	43
3.5.2	Characterization of <i>N</i> -acetylated-3-alkenyl oxindole derivatives.....	43
3.5.2.1	NMR Analysis	43
3.6	Antimicrobial activity of synthesized oxindole derivatives	43

3.6.1	Thin-layer chromatography (TLC)–bio autography technique.....	43
3.6.2	Agar well diffusion assay.....	44
3.6.3	Germ tube test method for the identification of clinical isolates of <i>C. albicans</i>	45
3.6.4	Broth micro-dilution assay against <i>Candida</i> species.....	45
3.6.4.1	Minimum inhibitory concentration by Resazurin assay	45
3.6.4.2	Minimum Fungicidal Concentration by drop culture method	47
3.7	Antioxidant activity	47
3.7.1	DPPH radical scavenging activity.....	47
3.7.2	ABTS radical scavenging assay	48
3.7.3	Ferric reducing antioxidant power (FRAP).....	48
3.8	Brine Shrimp lethality assay.....	49
RESULTS AND DISCUSSION		50
4.1	APTES-Silica	50
4.1.1	Preparation of APTES-Silica	50
4.1.2	Characterization of APTES-Silica	53
4.1.2.1	FTIR.....	53
4.1.2.2	Thermogravimetric analysis	54
4.1.2.3	Powder X-ray Diffraction	55
4.1.2.4	SEM Analysis	56
4.1.2.5	CHN analysis	57
4.2	Synthesis of 3-Alkenyl oxindole derivatives.....	58
4.2.1	Optimization of reaction conditions.....	58

4.2.2	Microwave assisted solvent-free synthesis of 3-Alkenyl oxindole derivatives.....	60
4.2.2.1	UV-Vis Spectra of synthesized 3-Alkenyl oxindole derivatives.....	60
4.2.2.2	NMR Analysis of synthesized 3-Alkenyl oxindole derivatives	63
4.2.3	Proposed reaction mechanism.....	66
4.2.4	Recyclability of the catalyst.....	67
4.2.5	Spectral data of synthesized 3-substituted indolin-2-ones.....	68
4.3	<i>N</i> -Acetylation of 3-Alkenyl oxindole derivatives using H ₂ SO ₄ -Silica.....	83
4.4	H ₂ SO ₄ -Silica.....	83
4.4.1	Characterization of H ₂ SO ₄ -Silica.....	83
4.4.1.1	FTIR.....	84
4.4.1.2	SEM Analysis	85
4.4.1.3	TGA Analysis	86
4.4.2	Acetylation reaction of 3-Alkenyl oxindole derivatives with H ₂ SO ₄ -Silica	87
4.4.2.1	UV-Vis spectra of synthesized <i>N</i> -substituted oxindole derivatives	87
4.4.2.2	NMR spectra of synthesized <i>N</i> -acetylated 3-alkenyl oxindole derivatives	90
4.4.3	Confirmation of acetylation of 3-Alkenyl oxindole derivatives	92
4.4.4	Spectral data of synthesized <i>N</i> -acetylated-3-alkenyl oxindoles.....	93
4.4.5	Proposed reaction mechanism.....	106
4.5	Antimicrobial Activity.....	107
4.5.1	Thin-layer chromatography (TLC)–bioautography for antimicrobial screening	107

4.5.2	Germ tube assay for clinical isolates of <i>Candida albicans</i>	108
4.5.3	Agar well diffusion assay	109
4.5.4	Minimum Inhibitory Concentration (MIC)/Minimum Fungicidal Concentration (MFC)	112
4.5.5	Structure and antimicrobial activity relationship	117
4.6	Antioxidant activity	119
4.7	Brine Shrimp lethality assay	132
CONCLUSIONS		134
REFERENCES		
APPENDICES		

LIST OF TABLES

Table 3.1: Chemicals (Sigma Aldrich, AR Grade)	30
Table 3.2: Solvents (AR Grade).....	30
Table 3.3: TLC solvent systems used to separate compounds.....	39
Table 4.1: Calculation of C/N ratio and APTES coverage based on CHN analysis	57
Table 4.2: Optimization of the reaction conditions for APTES-Silica	59
Table 4.3: Synthesis of 3-alkenyl oxindole derivatives from selected carbonyl compounds: Preferred configurations determined by NMR chemical shifts.	64
Table 4.4: Calculation of molecular formula based on CHN analysis.....	76
Table 4.5: Synthesis of <i>N</i> -acetylated-3-alkenyl oxindole derivatives; Preferred configurations determined by ¹ H NMR chemical shifts.	91
Table 4.6: Calculation of molecular formula based on CHN analysis.....	101
Table 4.7: Zones of Inhibition of compounds (3a-3g) against a selected panel of bacteria and <i>Candida</i> species	110
Table 4.8: In-vitro antifungal activity of compounds 3a-3g (MIC and MFC is expressed in µg/ml).....	113
Table 4.9: In-vitro antioxidant activity (EC ₅₀ values) of compounds by ABTS assay	127
Table 4.10: The percentage lethality of brine shrimp larvae against tested compounds after 24-hour exposure	133

LIST OF FIGURES

Figure 2.1: Chemical structure of 2-oxindole	5
Figure 2.2: Chemical structures of pharmaceutically important oxindole derivatives (I-X).....	7
Figure 2.3: Chemical structures of naturally occurring 3-alkenyl oxindole derivatives (I-VI)	8
Figure 2.4: Pharmaceutically important 3-alkenyl oxindole derivatives (I-IX).....	10
Figure 2.5: Oxindole derivatives with antimicrobial activity	12
Figure 2.6: 3-Alkenyl oxindole derivatives with antioxidant activity	14
Figure 2.7: Conventional and microwave heating mechanisms	20
Figure 2.8: Diagram of microwave heating mechanism	21
Figure 2.9: Tetrahedron structure of silicates	22
Figure 2.10: Three different silanol groups on the silica surface.....	23
Figure 2.11: Schematic diagram of silane reagents act as linkers	25
Figure 3.1: Modified domestic microwave oven	32
Figure 3.2: Extraction of silica from rice husk	33
Figure 3.3: Refluxing silica with HCl for activation	34
Figure 3.4: Synthetic pathway of 3-alkenyl oxindole derivatives	37
Figure 3.5: Diagram of 96 well plate with different concentrations of the tested compounds	46
Figure 4.1: Preparation of APTES functionalized silica preparation.....	51
Figure 4.2: (a) rice husk ash; (b) filtrate before acidification; (c) filtrate after acidification; (d) rice husk extracted silica	52

Figure 4.3: Synthesis of APTES functionalized silica.....	52
Figure 4.4: FTIR spectra: neat silica (a) and (b) APTES functionalized silica	53
Figure 4.5: TGA thermograms: neat silica (a) and (b) APTES modified silica.....	54
Figure 4.6: XRD Analysis: neat silica (a) and (b) APTES modified silica	55
Figure 4.7: SEM micrographs: (A, B) neat silica, (C) activated silica, (D) APTES modified silica.....	56
Figure 4.8: TLC of the isolated 3-alkenyl oxindole derivatives (3a-3g) [(a) Oxindole, (b) Aldehyde, (c) Isolated product].....	60
Figure 4.9: (a) compound 3a; (b) UV-Vis spectra of 3a	61
Figure 4.10: (a) compound 3b; (b) UV-Vis spectra of 3b.....	61
Figure 4.11: (a) compound 3c; (b) UV-Vis spectra of 3c	61
Figure 4.12: (a) compound 3d; (b) UV-Vis spectra of 3d.....	62
Figure 4.13: (a) compound 3e; (b) UV-Vis spectra of 3e	62
Figure 4.14: (a) compound 3f; (b) UV-Vis spectra of 3f.....	62
Figure 4.15: (a) compound 3g; (b) UV-Vis spectra of 3g.....	63
Figure 4.16: Structures of synthesized 3-alkenyl oxindoles	63
Figure 4.17: Rationale for the preferred E configuration of synthesized 3-alkenyl oxindoles.	65
Figure 4.18: Proposed reaction scheme for Knoevenagel condensation reaction catalyzed by APTES functionalized silica	66
Figure 4.19: Recyclability of the APTES modified silica catalyst in repeated cycles...	67
Figure 4.20: ¹ H NMR spectrum of compound 3a (CDCl ₃ , 400 MHz).....	68
Figure 4.21: ¹³ C NMR spectrum of compound 3a (CDCl ₃ , 100 MHz)	69
Figure 4.22: FTIR spectrum of compound 3a.....	69

Figure 4.23: ^1H NMR spectrum of compound 3b (CDCl_3 , 400 MHz)	70
Figure 4.24: ^{13}C NMR spectrum of compound 3b (CDCl_3 , 100 MHz).....	71
Figure 4.25: FTIR spectrum of compound 3b.....	71
Figure 4.26: ^1H NMR spectrum of compound 3c (CDCl_3 , 400 MHz).....	72
Figure 4.27: ^{13}C NMR spectrum of compound 3c (CDCl_3 , 100 MHz)	73
Figure 4.28: FTIR spectrum of compound 3c.....	73
Figure 4.29: ^1H NMR spectrum of compound 3d (DMSO-d_6 , 400 MHz).....	74
Figure 4.30: ^{13}C NMR spectrum of compound 3d (DMSO-d_6 , 400 MHz).....	75
Figure 4.31: FTIR spectrum of compound 3d.....	75
Figure 4.32: ^1H NMR spectrum of compound 3e (DMSO-d_6 , 400 MHz)	77
Figure 4.33: ^{13}C NMR spectrum of compound 3e (DMSO-d_6 , 100 MHz).....	77
Figure 4.34: FTIR spectrum of compound 3e.....	78
Figure 4.35: ^1H NMR spectrum of compound 3f (CDCl_3 , 400 MHz)	79
Figure 4.36: ^{13}C NMR spectrum of compound 3f (CDCl_3 , 100 MHz).....	79
Figure 4.37: FTIR spectrum of compound 3f	80
Figure 4.38: ^1H NMR spectrum of compound 3g (CDCl_3 , 400 MHz)	81
Figure 4.39: ^{13}C NMR spectrum of compound 3g (CDCl_3 , 100 MHz)	81
Figure 4.40: FTIR spectrum of compound 3g.....	82
Figure 4.41: FTIR spectrum of sulfuric functionalized silica.....	84
Figure 4.42: SEM images of H_2SO_4 -Silica	85
Figure 4.43: TGA thermogram: neat silica (a) and (b) sulfuric functionalized silica....	86
Figure 4.44: (a) compound 4a; (b) UV-Vis spectra of 4a	88
Figure 4.45: (a) compound 4b; (b) UV-Vis spectra of 4b.....	88
Figure 4.46: (a) compound 4c; (b) UV-Vis spectra of 4c	89

Figure 4.47: (a) compound 4d; (b) UV-Vis spectra of 4d.....	89
Figure 4.48: (a) compound 4e; (b) UV-Vis spectra of 4e	89
Figure 4.49: (a) compound 4f; (b) UV-Vis spectra of 4f.....	90
Figure 4.50: Structures of synthesized <i>N</i> -acetylated-3-alkenyl oxindoles.....	90
Figure 4.51: ¹ H NMR spectrum of compound 4a (CDCl ₃ , 400 MHz).....	94
Figure 4.52: ¹³ C NMR spectrum of compound 4a (CDCl ₃ , 100 MHz).....	94
Figure 4.53: FTIR spectrum of compound 4a.....	95
Figure 4.54: ¹ H NMR spectrum of compound 4b (CDCl ₃ , 400 MHz)	96
Figure 4.55: ¹³ C NMR spectrum of compound 4b (CDCl ₃ , 100 MHz)	96
Figure 4.56: FTIR spectrum of compound 4b.....	97
Figure 4.57: ¹ H NMR spectrum of compound 4c (CDCl ₃ , 400 MHz).....	98
Figure 4.58: ¹³ C NMR spectrum of compound 4c (CDCl ₃ , 100 MHz)	98
Figure 4.59: FTIR spectrum of compound 4c.....	99
Figure 4.60: ¹ H NMR spectrum of compound 4d (CDCl ₃ , 400 MHz).....	100
Figure 4.61: ¹³ C NMR spectrum of compound 4d (CDCl ₃ , 100 MHz).....	100
Figure 4.62: FTIR spectrum of compound 4d.....	101
Figure 4.63: ¹ H NMR spectrum of compound 4e (CDCl ₃ , 400 MHz).....	102
Figure 4.64: FTIR spectrum of compound 4e.....	103
Figure 4.65: ¹ H NMR spectrum of compound 4f (CDCl ₃ , 400 MHz)	104
Figure 4.66: ¹³ C NMR spectrum of compound 4f (CDCl ₃ , 100 MHz)	104
Figure 4.67: FTIR spectrum of compound 4f.....	105
Figure 4.68: Bioautography [(1) Oxindole, (2b) aldehyde, (3a) product] against [I] <i>C. albicans</i> , [II] <i>E. coli</i>	107

Figure 4.69: Germ tube formation; (A) <i>Candida albicans</i> ; (B, C, D) clinical isolates of <i>Candida albicans</i>	108
Figure 4.70: Zone of Inhibition of 3a-3g, (P) Miconazole and(N) 40 % propylene glycol; (I) <i>C. albicans</i> ; (II) <i>C. glabrata</i> ; (III) <i>C. parapsilosis</i> ; (IV) <i>C. krusei</i> ; (V) <i>C. albicans</i> clinical isolates 1; (VI) <i>C. albicans</i> clinical isolates 2; (VII) <i>C. albicans</i> clinical isolates 3.....	111
Figure 4.71: (a) Results of resazurin dye assay for the determination of MIC; (b) drop culture for determination of MFC against <i>Candida albicans</i>	113
Figure 4.72: (a) Results of resazurin dye assay for the determination of MIC; (b) drop culture for determination of MFC against <i>Candida glabrata</i>	114
Figure 4.73: (a) Results of resazurin dye assay for the determination of MIC; (b) drop culture for determination of MFC against <i>Candida parapsilosis</i>	114
Figure 4.74: (a) Results of resazurin dye assay for the determination of MIC; (b) drop culture for determination of MFC against <i>Candida krusei</i>	115
Figure 4.75: (a) Results of resazurin dye assay for the determination of MIC; (b) drop culture for determination of MFC against clinical isolates 1 of <i>Candida albicans</i>	115
Figure 4.76: (a) Results of resazurin dye assay for the determination of MIC; (b) drop culture for determination of MFC against clinical isolate 2 of <i>Candida albicans</i>	116
Figure 4.77: (a) Results of resazurin dye assay for the determination of MIC;(b) drop culture for determination of MFC against clinical isolate 3 of <i>Candida albicans</i>	116
Figure 4.78: Diagram showing antifungal activity and structure relationship of 3-alkenyl oxindole derivatives	119
Figure 4.79: Diagram showing the colour change of APTS and DPPH radicals upon exposure to an antioxidant (Pérez-Burilo et al., 2020).....	120

Figure 4.80: Typical Colour change observed in compounds from ABTS and DPPH assays.....	121
Figure 4.81: 3-Alkenyl oxindole derivatives (3a-3g) Ascorbic acid (P): Antioxidant activity colour change observed by ABTS, DPPH, FRAP assays	122
Figure 4.82: <i>N</i> -acetylated-3-alkenyl oxindole derivatives (4a-4f) Ascorbic acid (P): Antioxidant activity colour change observed by ABTS, DPPH, FRAP assays.....	123
Figure 4.83: Comparison of antioxidant activity at three different concentrations of 3-alkenyl oxindole derivatives (3a-3g) using ABTS assay	124
Figure 4.84: Comparison of antioxidant activity at three different concentrations of <i>N</i> -acetylated-3-alkenyl oxindole derivatives (4a-4f) using ABTS assay.....	125
Figure 4.85: UV-Vis spectra pure compound (a), compound after addition of DPPH (b) DPPH radical (c) at 517 nm	126
Figure 4.86: Percentage free radical scavenging activity of 3-alkenyl oxindole derivatives tested from ABTS assay	128
Figure 4.87: Percentage free radical scavenging activity of <i>N</i> -acetylated 3-alkenyl oxindole derivatives and ascorbic acid tested from ABTS assay	129
Figure 4.88: Schematic diagram of antioxidant activity and structural relationship of 3-alkenyl oxindole derivatives	131
Figure 4.89: (a) Brine shrimp larvae in control: (b, c) Brine shrimp larvae in samples	133

LIST OF SCHEMES

Scheme 2.1: Heck reaction in the synthesis of novel 3-alkenyl oxindoles	17
Scheme 2.2: Domino carbopalladation in the synthesis of 3-oxindoles.....	17
Scheme 2.3: Knoevenagel condensation in the synthesis of 3-alkenyl oxindoles	18
Scheme 2.4: Claisen–Schmidt condensation catalyzed by APTES-Silica	26
Scheme 2.5: Knoevenagel condensation catalyzed by APTES-Silica	27
Scheme 2.6: Acetylation of sugar molecule using H ₂ SO ₄ -Silica	27
Scheme 2.7: Acetylation of alcohols using H ₂ SO ₄ - Silica	28
Scheme 3.1: Typical reaction between oxindole and anisaldehyde	36
Scheme 3.2: Synthesis of 3-alkenyl oxindole derivatives (3a-3g)	38
Scheme 3.3: Synthesis of <i>N</i> -acetylated 3-alkenyl oxindole derivatives.....	42

LIST OF ABBREVIATIONS

APTES	3-Aminopropyltriethoxysilane
UV-Vis	Ultraviolet-Visible Spectroscopy
FTIR	Fourier Transform-Infrared
NMR	Nuclear Magnetic Resonance
SEM	Scanning Electron Microscopy
XRD	X-Ray diffraction
TGA	Thermogravimetric analysis
ATR	Attenuated total reflection
ATCC	American Type Culture Collection
<i>S. aureus</i>	<i>Staphylococcus aureus</i>
<i>P. aeruginosa</i>	<i>Pseudomonas aeruginosa</i>
<i>E. coli</i>	<i>Escherichia coli</i>
<i>C. albicans</i>	<i>Candida albicans</i>
MRSA	Methicillin Resistant <i>Staphylococcus aureus</i>
DPPH	(2,2-diphenyl-1-picryl-hydrazyl-hydrate)
ROS	Reactive oxygen species
DMSO	Dimethyl sulfoxide
CDCl ₃	Deuterated Chloroform
WHO	World Health Organization
TLC	Thin-layer chromatography
MHA	Mueller-Hinton agar
SDA	Sabouraud dextrose agar

SDB	Sabouraud dextrose broth
MIC	Minimum Inhibitory Concentration
MFC	Minimum Fungicidal Concentration

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Green Approach to Synthesis of Oxindole Derivatives and investigations of their
Antimicrobial and Antioxidant Activities

Hapuhinne Pallayage Shyamali Kumari Wijekoon

ABSTRACT

Synthesis of biologically active compounds in an environmentally benign manner is a challenge. This study reports the efficient synthesis of thirteen 3-alkenyl oxindole derivatives including two novel compounds in solvent-free condition under microwave irradiation. The synthetic procedure contains two consecutive steps. In the first step, seven 3-alkenyl oxindole derivatives were synthesized from oxindole and aromatic aldehydes in the presence of (3-aminopropyl)ethoxysilane (APTES) functionalized silica as a heterogeneous catalyst. Secondly, the synthesized oxindole derivatives were acetylated using acetic anhydride in the presence of H₂SO₄ functionalized silica to obtain *N*-acetylated 3-alkenyl oxindole derivatives. The silica was extracted from the rice husk ash under microwave irradiation and functionalized with APTES and H₂SO₄ to use as heterogeneous catalysts in above reactions. The catalysts were characterized by powder X-Ray diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), Thermo gravimetric analysis (TGA), Scanning electron microscopy (SEM) and elemental analysis. The synthesized compounds were characterized by ¹H and ¹³C Nuclear Magnetic Resonance, FTIR, UV-Visible spectrophotometry, melting point and elemental analysis. The antibacterial activity of all synthesized oxindole derivatives against *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC 25923), Methicillin-Resistant *Staphylococcus aureus* (clinical strain), *Pseudomonas aeruginosa* (ATCC 27853), *Acinetobacter baumannii* (clinical strain), and the antifungal activity against

Candida albicans (ATCC 10231), *Candida glabrata* (ATCC 90030), *Candida parapsilosis* (ATCC 22019), *Candida krusei* (ATCC 6258), three clinical isolates of *Candida albicans* were determined. The antioxidant activity was investigated using ABTS, DPPH and FRAP methods. Detailed structural characterization confirmed the formation of APTES functionalized silica, H₂SO₄ functionalized silica and the thirteen oxindole derivatives with sufficient yields (72% - 91%). Only the non-acetylated 3-alkenyl oxindole derivatives demonstrated antimicrobial activity against tested organisms and the highest antifungal activity was observed against *Candida albicans*. Among the tested bacterial species, zones of inhibition (ZOI) were observed only against Gram positive organisms. Minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) values of these compounds were detected from 2 µg/ml to 125 µg/ml against tested *Candida* species. Following the *N*-acetylation of synthesized 3-substituted oxindole derivatives, the resulted antimicrobial property was diminished. The antioxidant activity of all the synthesized compounds was detected with half maximum concentration (EC₅₀) of 7±0.7 µg/ml to 326±26 µg/ml. Selected compounds with potential activities were further evaluated for their toxicity and found to have no toxicity at these concentrations. The simple work-up procedure, mild conditions, recyclability of the catalyst, shorter reaction times and high yields were advantages of this green protocol. The results of this study emphasize that these compounds can be considered as potential lead compounds for development of antioxidant and antifungals against *Candida* species.

Keywords: Microwave-Assisted, Solvent-free, 3-Alkenyl oxindole derivatives,
Antifungal activity, Rice husk extracted silica