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# Oral electrospun multi-component membranous drug delivery systems

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To: School of Therapeutic Sciences Postgraduate Office

**Amendment of Dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand**
**Candidate: Rubina Perveen Shaikh (0401248X)**

In order to address the valid comments from the examiners made with reference to the dissertation submitted on 20/04/2012, the following amendments have been made:

**1) In order to address the issue of indicating *et al.* in the correct manner and font, all identified instances of *et al.* have been amended from:**

"et al." (i.e. non-italic font)

to

*"et al."* (i.e. italic font)

**2) In order to address the issue of the use of abbreviations, a list of abbreviations has been included in the dissertation on pages xlii to xliv as follows:**

## LIST OF ABBREVIATIONS

| | |
|---|---|
| 3-FR: | 3-formyl rifamycin |
| ACN: | acetonitrile |
| AMBER: | Assisted Model Building and Energy Refinements |
| ANOVA: | Analysis of Variance |
| ARVs: | Antiretroviral drugs |
| ATR-FTIR: | Attenuated Total Reflectance Fourier-Transform Infrared |
| AUC: | Area under the Curve |
| BET: | Brunauer-Emmett-Teller |
| BJH: | Barrett-Joiner-Halenda |
| CA: | cellulose acetate |
| CAP: | cellulose acetate phthalate |

CED: Cohesive energy density

CHT: chitosan

$C_{max}$: maximum plasma concentration

CMC: carboxymethylcellulose

$CO_2$: carbon dioxide

CYP3A4: Cytochrome P450 (CYP) enzyme type 3A4

DDS: drug delivery system

DEE: drug entrapment efficiency

DNA: deoxyribonucleic acid

DoE: Design of Experiments

DPH: diphenhydramine HCl

FCCCD: face-centered central composite design

FTIR: Fourier-Transform Infrared

FUR: furosemide

FW: formic water

GA: glutaraldehyde

GBI: Global Business Intelligence

GIT: gastro-intestinal tract

GORD: gastro-oesophageal reflux disease

GR: gastro-retentive

G-CSF: recombinant human granulocyte-stimulating factor

HCL: hydrochloric acid

HIV: human immunodeficiency virus

HPC: hydroxypropyl cellulose

IBS: irritable bowel syndrome

IHZ: isonicotinyl hydrazone

INH: isoniazid

IPN: interpenetrating polymeric network

LCST: lower critical solution temperature

MDDSs: mucoadhesive drug delivery systems

MDF: maximum displacement force

MMDDS: multi-component membranous drug delivery system

MMER: molecular mechanics energy relationship

MP: methylparaben

MRI: Magnetic Resonance Imaging

$M_w$: molecular weight

n: sample size

NAW: narrow absorption window

$N_2$: nitrogen

NT: nanotensile

OROS: osmotic-controlled release oral delivery system

OVAT: one-variable-at-a-time

PAA: poly(acrylic acid)

PBS: phosphate buffered saline

PDA: photodiode array

PEC: pectin

PEG: poly(ethylene glycol)

PEO: poly(ethylene oxide)

P(EVAL): poly(ethylene-co-vinyl alcohol)

P(NIPAAm): poly(N-isopropylacrylamide)

PVA: poly(vinyl alcohol)

PVDF: Polyvinylidene fluoride

PVP: polyvinylpyrrolidone

$R^2$: correlation coeffecient

RIF: rifampicin

RSM: response surface methodology

SD: standard deviation

SEM: scanning electron microscope

SGM: simulated gastric membrane

SIM: simulated intestinal membrane

SPE: solid phase extraction

$T_g$: glass transition temperature

TB: tuberculosis

TIPS: thermal-induced phase separation

TMC: trimethylated chitosan chloride

UPLC: ultra performance liquid chromatography

VIPS: vapour-induced phase separation

WA: work of adhesion

WAC: water absorption capacity

**3) In order to address the issue of indicating the sample size abbreviation in the correct manner as identified by the examiner, all identified instances of the abbreviation appearing in the dissertation have been amended from:**

“N=” (i.e. upper case font employed)

to:

“n=” (i.e. lower case font employed)

**4) In order to address the issue of citations of authors with surnames that include a prefix, all identified instances where the surname appears without the first name in the dissertation have been amended from:**

The incorrect use of lower case font, i.e. von Recum, du Toit

to

Use of upper case font for the prefix i.e. Von Recum and Du Toit.

**5) In order to address the issue of the incorrect use of upper case font when indicating generic names or active ingredients, all identified instances appearing in the dissertation have been amended from:**

use of upper case font when indicating Rifampicin and Isoniazid

to

use of lower case font when indicating rifampicin and isoniazid.

**6) In order to address the issue of not defining abbreviations on Page 1, Paragraph 1, the following sentence, appearing on Lines 6-8, has been amended from:**

“GBI Research has reported that oral drug delivery controlled 52% (R49bn) of the global drug delivery market share in 2009 and is expected to increase to R92bn by 2016”

to:

“Global Business Intelligence (GBI) Research has reported that oral drug delivery controlled 52% (R49 billion) of the global drug delivery market share in 2009 and is expected to increase to R92 billion by 2016.”

**7) In order to rectify the grammar error identified by the examiner on Page 2, Paragraph 2, the following sentence, appearing on Line 1, has been amended from:**

“In a highly competitive environment, there in an ongoing race for pharmaceutical industries to develop new drugs boasting improved bioavailabilities with a reduced side effect profile.”

to:

“In a highly competitive environment, there is an ongoing race for pharmaceutical industries to develop new drugs boasting improved bioavailabilities with a reduced side effect profile.”

**7) In order the ensure rectify the overlap issue of the text and text box identified by the examiner on Page 4, Figure 1.2, the fourth text box on the right has been resized, ensuring clarity of the reference.**

**8) In order to rectify the spelling error identified by the examiner on Page 17, Paragraph 4, Line 4:**

“…physical-chemical…”

was replaced with

“…physicochemical…”

**9) In order to rectify the spelling error identified by the examiner on Page 33, Paragraph 1, Line 11:**

“…paclitexal…”

was replaced with

"…paclitaxel…"

**10) In order to address the issue of poor sentence construction on Page 38, Paragraph 1, the following sentence, appearing on Line 11, was amended from:**

"These polymers are typically soluble in a solvent (usually water) at lower temperatures, and once the LCST has been reached, gel and are rendered insoluble at temperatures above the LCST."

to:

"These polymers are typically soluble in a solvent (usually water) at lower temperatures, however, once the LCST has been reached, the polymers begin to solidify and are rendered insoluble at temperatures above the LCST."

**11) In order to address the grammar error identified on Page 69, Paragraph 2, Line 3 was amended from**:

"Granted the formulations containing PVA still displayed mucoadhesive characteristics…"

to:

"Granted that the formulations containing PVA still displayed mucoadhesive characteristics..."

**12) In order to address the issue of incorrectly referring to the central composite design being rotatable as a result of α=1, the first sentence of Paragraph 3 on pPage 79 has been removed from the dissertation.**

**13) In order to address the issue of sample preparation with regards to FTIR analysis, the following sentence was added to Lines 3-5 of Paragraph 1 on Page 102:**

"Samples, requiring no modification, were placed in direct contact with the ATR crystal."

**14) In order to rectify the grammar error identified by the examiner on Page 120, Paragraph 1, Line 6:**

“agricultures”

was replaced with:

“agriculture”

**15) In order to rectify the spilling error identified by the examiner on Page 123, Paragraph 1, Line 6:**

“physiochemical”

was replaced with

“physicochemical”

**16) In order to address the issue of the use of the term “primordial” in Paragraph 1 of Page 128, the sentence appearing on Line 1 was amended from:**

“…was the primordial focus the current Chapter…”

to: “…was the principle focus of the current chapter…”

**17) In order to address the issue of the use of diphenhydramine HCl as a model drug during preliminary studies, the following sentence on Line 13-14 was amended from:**

“…DPH was initially employed in preliminary studies in order to cut costs associated with employing RIF and INH…”

to:

“…DPH was initially employed in preliminary studies not only to reduce costs associated with INH and RIF use, but also to ensure the versatility in application of the MMDDS in terms of drug incorporation…”

**18) In order to address the issue of the use of trade names for chemicals such as Tween and Span, without inclusion of their chemical name, the sentence appearing on Lines 7-8 of Paragraph 2, Page 141, has been amended from:**

"…Tween® 80 and Span® 80 uniLAB® (Merck Chemicals (Pty) Ltd, Wadeville, Gauteng, RSA…"

to:

"…Tween® 80 (polysorbate) and Span® 80 (sorbitan oleate) uniLAB® (Merck Chemicals (Pty) Ltd, Wadeville, Gauteng, RSA…"

**19) In order to provide justification for the use of a consistent shear rate of 100/s, the following sentence was included in Paragraph 2 of Page 158:**

"…The aforementioned shear rate was selected for comparative purposes only and a constant shear rate was selected to reduce sample variability…"

**20) In order to address the issue of quoting a reference that wasn't cited in Paragraph 3 of Page 186 the quotation marks around "…non-traditional biomedical tensile modifiers of polymeric nanofibres…" were removed, as the phrase was not being referenced from other published research, but rather from the discussion highlighted previously in the chapter.**

**21) In order to address the grammar issue highlighted by the examiner, in Line 7 of Paragraph 1 on Page 198,**

"…pigs' vitals…"

was replaced with

"...pigs' vital signs..."

**22) As highlighted by the examiner, Aulton, 2002 was cited in text on Page 187, but not included in the reference list. Therefore, the following reference for Autlon, 2002 was added to Page 216 of the dissertation:**

"…Aulton, M.E., (2002). Pharmaceutics: The Science of Dosage Form Design, Second Edition. Churchill Livingstone, Edinburgh, UK…"

I trust these amendments will meet with your approval.

Yours sincerely

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