THE EFFICACY OF A HERBAL COMPLEX (*Ginkgo biloba, Panax ginseng, Bacopa monerii and Rhodiola rosea)* IN THE MANAGEMENT OF EXCESSIVE DAYTIME SLEEPINESS

By

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A dissertation submitted in partial compliance with the requirements of the Master's Degree in Technology: Homoeopathy.

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DECLARATION

I, Sindisiwe Sthembile Mazibuko declare that this dissertation is present my own work in both conception and execution, unless explicitly acknowledged (including citation of published and unpublished sources).The work has not previously been submitted in any form to the Durban University of Technology or to any other institution for assessment or for any other purpose

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Sindisiwe S Mazibuko (student) **Date of signature**

Approved for final submission

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Dr D F Naude (supervisor) **Date of signature**

DEDICATION

This dissertation is dedicated to my late grandmother Mrs LM Mbatha, who was a pillar of strength, a mother, a friend and almost everything. This woman opened my eyes to Homeopathy and made me pursue this profession

You forever live in my Heart

To my daughter Zanentle Zwane, I hope that my learning curves become your inspiration and courage, that they teach you to be strong, bold, determined with success in mind and to persevere.

Mommy loves you

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ABSTRACT

BACKGROUND

Good sleep is essential to health, yet university students are sleep deprived due to later bedtime and experience sleepiness during the day (Patte *et al*., 2017), Sleepiness is referred to an increase propensity to fall asleep and excessive sleepiness and sleep disorders are common in our society today (Bittencourt *et al*., 2005). Previous research suggested that sleep can affect academic performance (Halik *et al*.2016), this is because students were observed falling asleep in university rooms (Eden, 2006). Brand *et al*., (2009) also mentioned that students feel sleepy during certain periods of the day especially during classes, during low stimulation and during car or bus rides.

AIM OF THE STUDY

The aim of the study was to determine the efficacy of a herbal complex (*Ginkgo biloba, Panax ginseng, Bacopa monerii & Rhodiola rosea)* in the management of excessive daytime sleepiness (EDS) in terms of Epworth sleepiness scale (John, 1991) and Stanford sleepiness scale (Hoddes *et al*, 1973).

METHODOLOGY

The study was conducted at the Durban University of Technology and 31 participants were chosen according to a specific inclusion and exclusion criteria. The sample was then randomly divided into an active group (herbal treatment) consisting of 21 participants and a placebo group of 10 participants. The measuring tools that were used were Epworth sleepiness scale (ESS) (Appendix C) and Stanford Sleepiness Scale (SSS) (Appendix D).

The initial consultation with the researcher consisted of signing the informed consent forms, case taking, physical examinations and filling in the ESS. Thereafter there were two follow up consultations; a week after the first consultation (the second consultation) at which point the treatment/placebo was dispensed and again two weeks from the second consultation which was the last day of the study and at which point medication containers were returned and final case taking and physical examinations were performed. The ESS was completed at recruitment, at the second consultation (both pre-treatment) and at close out and the SSS was completed for a period of three weeks (one week pre-treatment) and two weeks post treatment.

RESULTS

The data analysis methods that were used in the study were; Cronbach alpha score, One sample Kolmogorov-Simrnov test, Fisher's exact test, Pearson's correlation test, Independent sample test and ANOVA for ESS and mixed factorial ANOVA was used to evaluate the SSS.

In conclusion in terms of the ESS both groups improved significantly over time; degrees of improvement however were not statistically dissimilar although a review of mean scores indicates the active group as having lower scores suggesting a clinically significant trend.

SSS data however confirmed statistically significant differences between groups in favour of the active group confirming the herbal complex superior effect over placebo in the treatment of EDS.

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DEFINITION OF TERMS

Allopathic treatment

A term loosely applied to the practice of mainstream (orthodox) medicine (Gaier, 1991).

Ayurvedic medicine

Ayur means “life” and Veda means “science” An ancient system of natural and medical healing that originated in India (Gottlieb, 2000).

Complex

A simultaneous prescription of two or more remedies to treat a particular disease (O’Reilly, 2001).

Efficacy

The extent to which a specific intervention, procedure or regime does what it is intended to do for a specific population, when applied in ideal circumstances (Swayne, 2000).

Herb

A plant or part of the plant that is valued for its medicinal, savory, or aromatic qualities (Webster, 2017).

Homoeopathy

A therapeutic system based on the law of similar, where diseases are treated with substances that are able to produce, in a healthy person, symptoms similar to those displayed when ill (British Homoeopathic Association, 1992).

Placebo

A substance that has no therapeutic effect, used as a control in testing new drugs (Oxford Dictionary, 2017).

Population

An aggregate or totality of all the objects, subjects or members that conform to a set of specification (Polit and Hungler, 1999).

Sleepiness

The desire to fall and it is also referred to as a feeling of drowsiness that typically increases the longer we stay awake (Peters, 2016).

Sleep disorder

Are group of condition that affect the ability to sleep well on a regular basis, they may be caused by healthy problems or by too much stress (Roddick and Cherney, 2016).

Traditional pharmacotherapy

A science which focuses on the use of drugs to treat disease, it involves almost every branch of medicine (McMahon, 2017).

LIST OF ACRONYMS

ACRONYMS	FULL NAME
COPD	: Chronic Obstructive Pulmonary Disease
EDS	: Excessive Daytime Sleepiness
REM	: Rapid Eye Movement
NREM	: Non Rapid Eye Movement
ESS	: Epworth Sleepiness Scale
SSS	: Stanford Sleepiness Scale
DUT	: Durban University of Technology
WHO	: World Health Organisation
AASM	: American Academy of Sleep Medicine
ICSD-3	: International Classification of Sleep Disorders- 3rd edition
NSF	: National Sleep Foundation
OSA	: Obstruction Sleep Apnoea
FDA	: Food and Drug Administration

CHAPTER ONE

INTRODUCTION

1.1 The context of the study

Excessive Daytime Sleepiness (EDS) is the most common symptom reported by patients visiting sleep clinics; approximately 20% of adults in the USA have reported daytime sleepiness severe enough to impact negatively on daily activity (Pagel, 2009). The prevalence of EDS amongst university students has been well documented; Tsou (2014) reported a prevalence of 27% amongst students from two Taiwanese universities and established an association between EDS and emotional disturbances similarly high prevalence rates have been reported amongst university students in Peru (35%), Chile (28%), Ethiopia (26%) and Taiwan (27%) (Whittier *et al*. 2013; Concepcion *et al*. 2013; Robinson *et al*. 2013, Tran *et al*. 2013).

Pagel *et al* (2007) reports that sleepy adolescent students exhibit poorer academic performance, tardiness and have lower graduation rates, furthermore EDS compromises professional performance in both physicians (Chen *et al*. 2008) and judges (Grunstein, *et al*. 2007). Those experiencing cognitive decline associated with EDS are likely to be perceived as being lazy or unmotivated, which could ultimately prevent them being employed or loosing employment (Pagel, 2009).

Traditional pharmacotherapy using amphetamines, is problematic due to the high potential for abuse and common side effects (Pagel, 2009). Caffeine; although better tolerated may also be associated with toxicity signs such as nervousness, irritability, insomnia and GIT disturbances (Banerjee *et al*. 2004), Ironically the use of Caffeine by university students in the form of energy drinks was associated with increased odds of daytime sleepiness (Tran *et al*. 2013, Whittier, *et al*. 2013).

Although no formal studies on EDS amongst tertiary education students in South Africa could be sourced, anecdotal evidence as well as the observations of the researcher suggests that EDS is a common phenomenon amongst students at Durban University of Technology.

Herbal medicine such as *Ginkgo biloba, Panax Ginseng, Bacopa monerii and Rhodiola rosea* have each been extensively researched and proven efficacious in a number of related fields. *Ginkgo biloba* has demonstrated efficacy with regard to Attention Deficit Hyperactivity Disorder (Niederhofer 2010), improved cerebral blood flow (Mashayekh, Pham *et al*. 2011), improved selective attention, working memory and cognitive flexibility as well as long term memory for verbal and non-verbal material (Kaschel 2009).

Panax ginseng (Korean Ginseng) is well known in herbal medicine as an adaptogen and tonic and used for physical and mental exhaustion as well as stress and has demonstrated clinical efficacy regarding improved performance, general wellbeing and mental health (Morgan and Bone 2008), fatigue, insomnia and depression (Tode, Kikuchi *et al*. 1999) general wellbeing (Wiklund, Mattsson *et al*. 1999) and aspects of working memory performance (Reay, Scholey *et al*. 2010). *Bacopa monerii* significantly improves memory acquisition and retention (Morgan and Stevens 2010) and improves cognition in particular the speed of attention (Kongkeaw, Dilokthornsakul *et al*. 2014).

Rhodiola rosea is used in herbal medicine traditionally enhance mental and physical performance and immunity and is classified as an adaptogen (Morgan and Bone 2008). It has demonstrated efficacy with regard to physical fitness mental fatigue and neuro-motoric tests and improved general well-being in fatigued students during exam periods (Spasov, Wikman *et al*. 2000). In addition, healthy doctors experienced improvement in mental performance and a reduction in general fatigue in response to *Rhodiola rosea* during night duty (Darbinyan, Kteyan *et al*. 2000).

Morgan and Bone (2008) suggest that *Rhodiola rosea* and *Panax ginseng* complement each other and may produce a synergistic effect for the treatment of fatigue and exhaustion, enhancing of mental performance including memory, concentration especially when under stress. Although there is significant evidence of the efficacy of the above mentioned herbal medicines no study could be sourced which measured the efficacy of this unique combination of herbal medicines, it was anticipated that this specific combination would be efficacious in the management of EDS.

1.2 The aim of the study

The aim of this randomised, double-blind placebo controlled study was to determine the efficacy of a herbal complex (*Rhodiola rosea, Gingko Biloba, Panax Ginseng & Bacopa monerii)* in the management of excessive daytime sleepiness in terms of the Epworth Sleepiness Scale (Johns 1991) and Stanford Sleepiness Scale (Hoddes, Zarcone *et al*. 1973).

1.3 The objectives of the study

Objective 1: To determine the efficacy of a herbal complex *Rhodiola rosea, Gingko Biloba, Panax Ginseng & Bacopa monerii)* in the management of EDS in terms of the Epworth Sleepiness Scale (ESS).

Objective 2: To determine the efficacy of a herbal complex (*Rhodiola rosea, Gingko Biloba, Panax Ginseng & Bacopa monerii)* in the management of EDS in terms of the Stanford Sleepiness Scale (SSS).

1.4 Statement of hypotheses

1.4.1 The first hypothesis

It was hypothesised that a herbal complex (*Rhodiola rosea, Gingko Biloba, Panax Ginseng and Bacopa monerii)* would have a beneficial effect in the management of Excessive Daytime Sleepiness (EDS) in terms of the Epworth Sleepiness Scale (Appendix D)

1.4.2 The second hypothesis

It was hypothesised that a herbal complex (*Rhodiola rosea, Gingko Biloba, Panax Ginseng and Bacopa monerii)* would have a beneficial effect in the management of Excessive Daytime Sleepiness (EDS) in terms of the Stanford Sleepiness Scale (Appendix C)

1.5 Delimitations of the study

- The sample size of this study was small (n=31) largely due to budgetary limitations and the scope of a coursework mini-dissertation
- The study was limited to tertiary students within KwaZulu-Natal
- The study was limited to participants between the age of 18-30 years
- The study was limited to participants with no other medical conditions
- The student did not attempt to explain or postulate the neurological origin of the EDS amongst students

1.6 Assumptions of the study

1. Participants took the medication as prescribed
2. Participants graded themselves (SSS) hourly
3. Participants took only the prescribed medication during the study and no other interventions for EDS
4. Blinding was maintained throughout the study

CHAPTER TWO

REVIEW OF THE RELATED LITERATURE

2.1 Introduction

10% of world's population has diagnosable sleep disorders, this was estimated by the American Academy of Sleep Medicine (AASM). The majority of sleep disorders are treatable but there is lack in education and training. This leads to disorders not being detected by medical professionals (AASM, 2017). Research conducted on resident physicians in the US showed that excessive working hours lead to restricted sleep and fatigue, causing high rates of medical errors, motor vehicle accidents, reduced motivation, increased irritability and increased depression (Ayas *et al*, 2006). Reduced sleep time, later bedtime and wakening, irregular sleep/wake patterns and poor sleep quality also have a negative impact in academic performance (Wolfson and Carskadon, 2003).

According to Gaultney (2016) excessive daytime sleepiness may be a factor contributing torwards poor performance. Excessive daytime sleepiness also poses a wide range of adverse health related outcomes in older people, such as disability which impairs everyday activities and may increase the risk of falls (Lima *et al*, 2015).

2.2 Physiology of sleep

The mechanism of sleep-wake cycle, which consists of about 8 hours of nocturnal sleep and 16 hours of wakefulness during the day in humans, is controlled by the combination of sleep homeostasis and circadian rhythms (National sleep foundation, 2006).

Homeostasis controls the amount of sleep at night and maintains the blood pressure, body temperature and acid-base balance at a steady state. When we wake up, the homeostatic drive for sleep accumulates to reach its maximum in the late evening when the majority fall asleep. When we are awake, blood levels of adenosine increases and results in a growing need for sleep that become less resistible over time. Adenosine receptors can be blocked by caffeine preventing the need of feeling sleepy, which is where sleep is lost. The body will start to demand that makeup of lost sleep for each hour which results in a very negative effect on daytime performance, thinking and mood (National sleep foundation, 2006).

Circadian rhythms are driven by the brain's biological clock which consists of group of neurons in the hypothalamus (suprachiasmatic nucleus). The internal 24 hour rhythms are synchronized to the external physical environment and social/work schedules, human light is the strongest synchronizing agent as the light and darkness are external signals that set the biological clock and determine when do we wake up or go to sleep (National sleep foundation, 2006).

Homeostatic systems make us fall asleep as time goes on regardless of whether its night or during the day, while the circadian rhythms keep us awake during the day and make us go to sleep as soon as it become dark. When circadian rhythms are disrupted; mental and physical performance is diminished (National sleep foundation, 2006).

There are two types of sleep, non-rapid eye movement (NREM) and rapid eye movement (REM) (National sleep foundation, 2006).

2.2.1 NREM sleep

NREM sleep comprises four stages:

Stage 1

This is the stage where drowsiness is experienced i.e. human brain waves and muscle activity start to deteriorate and concentration is decreased and an individual suddenly begins to fall asleep (National sleep foundation, 2006).

Stage 2

During the second stage, eye movements stop and an individual enters a period of light sleep. There is further reduction of brain waves with sleep spindles (rapid waves), accompanied by periods of muscle tone combined with periods of muscle relaxation. Research has also shown that there is decreased heart rate and body temperature at this stage (National sleep foundation, 2006).

Stage 3 and 4

These stages are known as slow wave sleep because of their slow brain waves called delta waves intermixed with smaller, faster waves. Physiologically blood pressure decreases, body temperature and breathing rate is lowered and the body becomes motionless (National sleep foundation, 2006).

During these stages sleep is deeper, and it is more challenging to be awakened; if one is woken at this stage there may be a transient feeling of grogginess and disorientation. It is during this phase that conditions such as bedwetting, night terrors or sleepwalking occur (National sleep foundation, 2006).

2.2.2 REM Sleep

This is the active period of sleep that is marked by powerful brain activity. Brain waves are fast and similar to those of the wake state, breathing rate is found to be rapid, irregular and shallow and heart rate and blood pressure increases. Temporary paralysis of limb muscles and fast movement of the eyes to different directions is experienced; this is the common time at which most dreams take place (National sleep foundation, 2006).

2.3. Classification of sleep disorders

The American Academy of Sleep Medicine classified sleep disorders into 6 main categories as follows:

2.3.1 Insomnia

The International Classification of Sleep Disorder-3 (ICSD-3) describes insomnia as a persistence difficulty of initiating or maintaining sleep which might be due to consolidation or quality that occurs despite adequate opportunity and circumstances for sleep and results in some form of daytime impairment (AASM, 2014).

Phillips (2015) groups insomnia into 4 major categories:

- Chronic insomnia disorder
- Short-term insomnia disorder
- Other insomnia disorders
- Isolated symptoms and normal variant

Insomnia ranges from mild to severe, mild being a nightly complaint of an insufficient amount of sleep or not feeling rested after the habitual sleep episode, with little or no evidence of impairment on social occupational function and it often associated with feeling of restlessness, irritability, mild anxiety, fatigue and tiredness. Moderate insomnia is always associated with the symptoms mentioned above and those with severe insomnia

have severe social impairment associated with feeling of restlessness, irritability, mild anxiety, fatigue and tiredness (Buysse, 1997).

2.3.2 Sleep related breathing disorder (Zucconi and Ferri, 2014)

These are conditions characterized by disordered respiration during sleep and include the following:

- Obstructive sleep apnoea
- Central sleep apnoea
- Sleep-related hypoventilation disorder
- Sleep-related hypoxemia disorder

2.3.3 Central disorders of hyper somnolence (Zucconi and Ferri, 2014**)**

This is the inability to stay awake and alert during the major episodes of wakefulness during the day, resulting in periods of involuntary bouts of drowsiness or sleep.

- Narcolepsy type 1
- Narcolepsy type 2
- Idiopathic hypersomnia
- Kleine- levin syndrome
- Hypersomnia due to a medical disorder or medical substance
- Hypersomnia associated with psychiatric disorder
- Insufficient sleep syndrome

2.3.4 Circadian rhythm sleep-wake disorder (Zucconi and Ferri, 2014)

These are the disorders that include conditions in which sleep times are out of alignment and include:

- Delayed sleep-wake phase disorder
- Advanced sleep-wake phase disorder
- Irregular sleep-wake rhythm disorder
- Non-24h sleep-wake rhythm disorder
- Shift work disorder
- Jet lag disorder

- Circadian sleep-wake disorder not otherwise specified

2.3.5 Parasomnia (Zucconi and Ferri, 2014)

These are disorders that are characterized by occurrence of complex motor or behavioural events and usually take place within sleep or during arousal from sleep.

- NREM related:
  Disorders of arousal
    - Confusion arousal
    - Sleepwalking
    - Sleep terrors
    - Sleep related eating disorder
- REM related:
  REM sleep behaviour disorder
    - Recurrent isolated sleep paralysis
    - Nightmare disorder
- Other:
    - Exploding head syndrome
    - Sleep-related hallucinations
    - Sleep enuresis
    - Parasomnia due to medical disorder
- Isolated symptoms and normal variants: sleep taking

2.3.6 Sleep related movement disorder (Zucconi and Ferri, 2014)

This is the stereotype movements that occur during sleep or at its onset and includes:

- Restless leg syndrome

- Periodic limb movement
- Sleep related leg cramp
- Sleep related bruxism
- Sleep related rhythmic movement disorder
- Benign sleep myoclonus of infancy
- Propriospinal myoclonus at sleep onset
- Sleep related movement due to a medical condition disorder
- Sleep related movement disorder, unspecified
- Sleep starts (hypnic jerks)
- Isolated symptoms and normal variants: excessive fragmentary myoclonus, Hypnagogic foot tremor and alternating leg muscle activation

2.4. Excessive daytime sleepiness (EDS)

Excessive daytime sleepiness is a secondary symptom of sleep disorders, characterised by difficulty in remaining awake in the wake period and is usually related to sleep disturbances, inclusive of obstructive sleep apnoea, narcolepsy and idiopathic hypersomnia. It is also said to be related to poor health status, low physical activity levels, disability in daily activities and an increased number of depression symptoms (Lima *et al*, 2015).

EDS is of high clinical and public health importance, 16% of motor accidents, 50% of work related accidents and 25% of home based accidents are linked to EDS. It has been said to be associated with psychiatric and medical conditions, even though its neurobiology is not well understood (Meyer *et al.*, 2011).

2.5. Incidence and prevalence of EDS

EDS is the most common symptom reported by patients visiting sleep clinics; approximately 20% of adults in the USA have reported daytime sleepiness severe enough to impact negatively on daily activity (Pagel, 2009). The prevalence of EDS amongst university students has been well documented; Tsou (2014) reported a prevalence of 27% amongst students from two Taiwanese universities and established an association between EDS and emotional disturbances. Similarly high prevalence rates have been reported amongst university students in Peru (35%), Chile (28%), Ethiopia (26%) and

Taiwan (27%) (Whittier *et al*. 2013; Concepcion *et al*. 2013; Robinson *et al*. 2013, Tran *et al*. 2013).

Ramamoorthy *et al*. (2014) reported the prevalence of EDS among medical students in the Southern part of South India; the overall prevalence was 30.57%, 52.06% were males and 47.10% were females suggesting that females have better sleep quality than males. The prevalence of EDS was 12% in Americans, 2.5% in Japanese, 4.5% in Korean men and 3.2% in Korean females (Roth and Roehrs, 1996; Kaneita *et al.*, 2005; Kim *et al.*, 2004). The prevalence of EDS amongst medical students has been documented as being 39.5% in Brazilian medical students (Rodrigues *et al*., 2002), 35.5% in Malaysian medical students and 17.3% in medical students in the Northern part of India (Zailinawati *et al.*, 2009).

2.6. AETIOLOGY OF EDS

According to Banerjee *et al*., (2004) the following are causes of EDS:

- Intrinsic sleep disorders such as narcolepsy, obstructive sleep apnea and idiopathic hypersomnia.
- Extrinsic sleep disorders such as inadequate sleep hygiene, insufficient sleep syndrome and toxic- induced sleep disorder.
- Circadian rhythm sleep disorders such as delayed sleep phase syndrome and time zone change syndrome
- Sleep disorders associated with medical and mental disorders

The American National Sleep Foundation (NSF) reported that 59% of adults that described themselves as night owls were between the age of 18 to 29 years, as they were not able to fall asleep earlier in the evening and they cannot get enough sleep if they must wake up early. Reduced sleep time, later bedtime and awakening, irregular sleep/wake patterns and poor sleep quality play a major role towards EDS (Wolfson and Carskadon, 2003).

Sleep may be voluntarily sacrificed due to social factors and compromised due to poor sleep hygiene such as noisy living conditions. In addition, college students are in their older adolescent years and are still dealing with adolescent physiology such as biological driven delayed sleep phase (Gaultney, 2010). Banks and Dinges (2007) reported that EDS can be a result of medical conditions and sleep disorders, as well as lifestyle (shift work, jet lag and prolonged work hours etc.).

Sleepiness in students depend on a variety of circumstances, a lecture that does not require active participation and lecture halls that are dark and warm especially in the afternoon, are some of the factors that contribute towards sleepiness. According to Hershner and Chervin (2014) 70,6% students reported to have of less than 8 hours of sleep per night and others often 'pulled an all-nighter' which means that they stay awake all night. Some of the factors that contributed towards sleep deprivation and sleepiness were: poor sleep behaviour (not having a regular sleep-wake schedule), being in a noisy sleep environment and taking stimulant after lunch or before bed. Consuming caffeine and energy drinks in the afternoon subsequently impaired the ability to fall asleep later. The study also revealed that technology had a negative impact on sleep hygiene; 67% college students were using cell phones, 43% were using music devices, 60% were using computers and 18% played video game prior to going to bed and wake up enrefreshed. Approximately four out of five students were drinking alcohol, which shortens sleep latency, but promotes fragmented sleep in the latter half of the night (Hershner and Chervin, 2014).

2.7. RISK FACTORS OF EDS

In the study conducted by Haglow *et al*., (2006) important risk factors for daytime sleepiness and fatigue amongst woman included snoring (obstructive sleep apnoea), insomnia and a lower mean sleep sufficiency index. Lifestyle factors identified included being overweight or obese with low physical activities, smoking, use of alcohol and both anxiety and depression combined.

Student and nightshift workers are at high risk of EDS and the incidence of different somatic diseases such as asthma or COPD, back or joint pain, fibromyalgia, diabetes, cardiovascular diseases and neurologic problems were said to be related to EDS (Haglow *et al.*, 2006). Short sleep duration and insomnia are well known predictors of EDS and fatigue (Haglow *et al.*, 2006).

2.8. SIGNS AND STMPTOMS OF EDS

As reported by Morrison *et al*. (2012) the following are signs and symptoms of EDS:

- Fatigue, which can relate to problems with energy, poor concentration and perceived muscle strength or mood
- Overwhelming need to sleep
- Unintended/mistakenly falling asleep
- Amnesia
- Automatic behaviour
- Impaired alertness performance
- Feeling of drowsiness

Patients suffering from EDS will typically have to expend a greater effort in order to remain awake during the day; this is the first symptom to develop accordingly. They will suffer attacks of falling asleep involuntarily, try to fight off sleepiness and refuse to take a nap however ultimately they are overcome by sleepiness without any warning. Some of the patients may suffer from micro sleeps without being conscious of having slept, or when engaged in a conversation can even drift into sleep in less than 30 seconds. EDS can also cause other symptoms like mental fuzziness, poor memory, problems with focusing the eyes, lack of energy and exhaustion (Doghramji, 2014).

2.9. COMPLICATIONS OF EDS

EDS affects 20% of the population in the United State and those who have this condition are at risk of motor vehicle and work-related incidents and have generally poorer health. EDS contributes toward more than 100 000 motor vehicle incidents, 71 000 personal injuries and 1 500 deaths annually; up to 52% of single vehicle crashes involving heavy trucks are fatigue-related because of the drivers falling asleep while driving (Pagel 2009).

Pagel *et al* (2007) reports that sleepy adolescent students exhibit poorer academic performance, tardiness and have lower graduation rates, furthermore EDS compromises professional performance in both physicians (Chen *et al*., 2008) and judges (Grunstein, *et al*., 2007). Those experiencing cognitive decline associated with EDS are likely to be perceived as being lazy or unmotivated which could ultimately prevent them being employed or result in them loosing employment (Pagel, 2009).

2.10. ASSESSMENT AND QUANTIFICATION OF EDS

2.10.1. The Epworth Sleepiness Scale (ESS) (Johns 1991)

The ESS is an inexpensive and simple EDS test that can be conducted within 5 minutes, which has been useful and was found to be dependable in numerous studies where individuals had to rate from a scale of 0-3 how likely will they doze off in eight different scenarios encountered on daily life; total scores can range from 0-24 and a score of greater than 16 suggests excessive daytime sleepiness (Johns, 1992).

An ESS score of less than 10 is considered to be normal daytime sleepiness (Mahoney *et al.*, 2014) and a total score obtained across the eight items that is greater than 10 is used to represent an abnormal level of daytime sleepiness (Baldwin *et al.*, 2004) and warrants further medical assessment (Doneh, 2015). Subjects may over score or underscore but any score above 10 is an indicator of EDS (on an individual basis). Sometimes the ESS scores are not clear in term of health outcomes; however the scale (ESS) remains a popular questionnaire due to its simplicity and brevity (Banerjee, 2007). With respect to validity and reliability of this tool, there were high levels of internal consistency between the eight situations accessed in the ESS as measured by Cronbach's Alpha, ranging from 0.74 to 0.88 and many other studies supported high validity and reliability of this measurement tool (Johns, 1992).

The ESS score of greater or equal to seven concluded 75% of incidents of sleeping while driving, with ESS having a degree of susceptibility of 70% and specificity of 52% (Kumar *et al.*, 2010).In addition, the ESS was also found to be sensitive to the changes produced by treatments for sleep apnoea (Shahid *et al.*, 2010).

According to Ramilo (2015), there was evidence of validity of total ESS scores, based on the experimental findings that ESS scores differ between normal subjects and patients with obstructive sleep apnoea (OSA) (known to increase sleepiness). The high ESS score of patients who suffered from OSA returned to normal after a successful treatment of their disorder by use of nasal continuous positive airway pressure treatment supporting the validity of this instrument (Ramilo, 2015).

The ESS alone cannot diagnose the nature of any sleep disorder, it is also not suitable for measuring rapid changes in sleep propensity over periods of hours, and for example ESS

cannot demonstrate the sedative effect of a single dose of a drug or to reveal a circadian rhythm of sleepiness (Ramilo, 2015).

In a study of 42 participants (13 females and 29 males), with the average age of 23 and BMI of 26,2, 11 of the participants were not on medication due medical reasons and the remaining 31 were separated into two groups of sleepy and alert. Alert participants were those with an ESS score of 1 to 6 while the sleepy had a score of more than nine in addition the alert group had a greater mean of sleep length and sleep efficiency than those of the sleepy group (Ramilo, 2015).

An investigation comparing healthy medical students and patients with OSA showed that the healthy medical students had a wide range of ESS scores that did not change over a period of five months, the high ESS score was indicative of excessive daytime sleepiness in patients with OSA were shown to return to normal as expected after a few months' treatment with nasal continuous positive airway pressure. These results provide evidence that the ESS is a simple and reliable method for measuring the general level of daytime sleepiness in adult (John, 1992).

2.10.2 The Stanford Sleepiness Scale (SSS) (Hoddes, Zarcone *et al*. 1973)

The SSS self-rating scale is known to be the broadest, quickly used subjective sleepiness measuring instrument and is administered at two hour intervals during the day (Shahid *et al.,* 2010). It consists of a seven-point scale of equal intervals starting from one (being very alert) to seven (being excessive sleepy) (Herscovitch and Broughton, 1981). It was found to cross-validate with performance when mental tasks were long, boring and being repeated. In the absence of high interest, incentives and motivation, these tests suggested most sensitive to sleepiness (Hoddes *et al*, 1973).

The SSS is not sensitive to distinguish between sleep apnoea participants and normal sleepers as the studies suggest that the SSS is sensitive with patients suffering from sleep disorders and tend to deny sleepiness, but it is known to be a useful sleepiness measuring scale for patients with narcolepsy (Shahid *et al*, 2010).

The SSS was the first self-rating scale found to be reliable and useful in determining the levels of sleepiness. SSS ratings were found to correlate significantly with performance on tasks which have been revealed to be sensitive to moderate amounts of sleep loss, and

this can be regarded as good indicators of sleepiness. The SSS may reflect useful information on insomnia, drug effects and most importantly clinical state in disorders associated with sleep, despite the absence the laboratory test or physiological changes. Recently it has been discovered the SSS to be of significant diagnostic value in the evaluation of insomniacs and narcoleptics (Hoddes *et al*, 1973).

A study on the Pupillographic assessment of sleepiness in sleep-deprived healthy subjects applied the SSS as their assessment tool. When the power of slow pupillary oscillations increased the SSS values also increased while basic pupil diameter decreased significantly. The researchers concluded that there was a strong relationship between on-going sleep deprivation and typical changes in the frequency profile of spontaneous papillary oscillations and tendency to instability in normal pupil size. The result reveals that the outcomes of pupil data analysis permit an objective measurement of sleepiness (Wilhelm *et al*, 1998)

In another study of 20 subjects with a history of mild snoring, the SSS was used as an evaluating questionnaire; it revealed a 26% reduction in daytime sleepiness at the end of the study (Scharf *et al*, 1994). Acute sleepiness in car drivers significantly increases the risk of motor vehicle accidents (MVA); this was shown by the strong relationship between the levels of acute driver sleepiness as measured by SSS and the risk of MVA (Cannor *et al*, 2002)

2.11. Treatment of EDS

2.11.1. Orthodox treatment (Pharmacotherapy):

Modafinil (Provigil) and Armodafinil (Nuvigil) are wakefulness promoting agents that are approved by the United States Food and Drug Administration (FDA) for treating sleeping disorders. It is normally taken in one or two doses in the morning and at midnight, not recommended to be taken in the afternoon because of its long half-life (15 hours). It is known to cause headaches, nausea, nervousness, dizziness, stuffy nose, dry mouth, anxiety, diarrhoea, chest pain, chills and a flu-like syndrome as possible side effects and is contraindicated in people with cirrhosis, cardiac conditions and hypersensitivity to the drug constituents (Taylor and Keys, 2003).

Methylphenidate which activates the sympathetic and central nervous system, keeps a person awake and improves mental activity. It is best known for treating Attention Deficit Disorder, Attention Deficit Hyperactivity Disorder and narcolepsy. Long term use of the medication may result in high blood pressure, irritability, tremors, mood swings, and difficulty in breathing, aggression, panic, numbness, fever, painful erections, weight loss, drowsiness and insomnia. Methylphenidate containing drugs should not be taken during pregnancy and breastfeeding or by patients with glaucoma, severe anxiety and tension and in those with a personal or family history of tics (Steele *et al*, 2006).

Sodium oxybate is central nervous system depressant used to avoid attacks of cataplexy, and excessive daytime sleepiness in patients suffering from narcolepsy. Sodium oxybate may cause side effects like bedwetting, headache, dizziness, feeling drunk, shaking of body parts, numbness, tingling, pricking sensation, nausea, vomiting, diarrhoea, back pain and swelling of the arms. It is contraindicated in patients taking antidepressants, medication for mental illness, seizures, insomnia, and sedatives (Frucht et al.2005).

Traditional pharmacotherapy using amphetamines is problematic due to the high potential for abuse and common side effects (Pagel, 2009), Caffeine although better tolerated may also be associated with toxicity signs such as nervousness, irritability, insomnia and GIT disturbances (Banerjee *et al*. 2004), Ironically the use of Caffeine by university students in the form of energy drinks was associated with increased odds of daytime sleepiness (Tran *et al*. 2013, Whittier, *et al*. 2013).

2.11.2. Herbal medicine

Rhodiola rosea

Also known as Artic or Golden Root from the *Crassulaceae* family, *Rhodiola* is traditionally used as an analeptic, to improve mental and physical performance in countries like Russia, Scandinavia and middle Asia. It was well known for its ability to increase physical endurance, reduce depression symptoms, to work on nervous system disorders and to reduce mental fatigue in students during examination periods (Morgan et al 2008).

In a clinical study, it displayed a major effect on cognitive cerebral functions increasing the ability of thinking, calculating and concentration with no adverse effects throughout the study and the results also revealed the reduction of fatigue under stressful conditions (Darbinyan et al. 2000). Kilham (2012) stated that *Rhodiola rosea* had a reputation of helping the body deal with occasional stress, fatigue and boosting general health and wellness. Recently, it is used to protect and reduce the appearance of fine lines and wrinkles and rejuvenate the skin, while it internally used to treat anaemia, erectile dysfunction, stomach upset and depression.

A recent study has proven that it helped those who were suffering from stress related fatigue by increasing their mental performance, decreasing levels of the stress related hormone cortisol in their blood, increasing energy levels and improving mood (Kilham, 2012). Group (2014) describes *Rhodiola rosea* as a herbal remedy for fatigue, anxiety and mood imbalance as it helps the body and mind to adapt to stress. A clinical trial conducted by Russian researchers in 2011 found that participants who were on *Rhodiola* supplements often experienced physical and mental rejuvenation.

In a study conducted by Eastern European researchers the participants who took *Rhodiola* reported having more energy and focus (Group, 2014). According to Group (2014) 120 adults who were experiencing physical and cognitive deficiencies participated in a 12-week study of *Rhodiola* combined with minerals and vitamins, there were positively reported changes in their physical and cognitive function and 80% of the test subjects rated very good effects and 99% of physician and patients believed the supplement to be safe.

According to Bystritsky et al. (2008) there are no serious side effects caused by *Rhodiola* except for mild to moderate symptoms of dizziness and dry mouth while Ishaque *et al*., (2012) reported minor and serious headaches as well as insomnia as side effects. The only documented contraindication to Rhodiola is bipolar mood disorder, although it may be beneficial in monopolar depression (Ishaque *et al*. 2012).

According to Bone (2007) the recommended dosing of Rhodiola is 20 to 40 ml/week (2:1 liquid) or 6 to 12 g/day tablet.

Ginkgo Biloba

Ginkgo has been a well-known treatment in Chinese medicine for various psychological conditions; it was taken as a supplement to sharpen the ability to think, for memory improvement and working on daily activities such as mood and emotional functions its method of action is believed to be the increase of blood flow to the brain (Kaschel, 2009). According to Kaschel (2009) it was effective in maintaining and recalling verbal and non-verbal information, in increasing the speed and processing of short and long term information and also played a role in executive functions (planning, flexibility, alertness, intelligence and working memory

As herbal medicine, it is used to avoid the relapse of cognitive functions and as a dietary supplement to increase cerebral blood flow in people with dementia (Mashayekh et al., 2011). Bone (2014) describes *Ginkgo* as a herb that sharpens memory and concentration, this is because of the support it provides, i.e. to support memory and cognition, healthy mental function, good health in older adults, normal hearing and eye health. It also promotes alertness and mental clarity, maintains healthy tissue fluid levels (especially in the legs), encourages healthy blood, provides antioxidant activity to help protect nerve cells, modulates cortisol during periods of stress, reduces the congestive symptoms of premenstrual syndrome and helps maintain proper energy and assists mood in times of stress.

It can be used in complex to obtain optimal wellbeing; enhanced mental clarity and support cognitive function when combined with Bacopa; it promotes healthy blood vessels and supports the body's normal tissue repair when combined with *Gotu Kola* (Bone, 2014)

Ginkgo has the tendency of increasing the risk of bleeding, inhibiting platelet aggregation by increasing concentration of endothelium- derived thrombolytic, inhibiting the binding of platelet-activating factor to its receptors on platelet membranes and affecting the interactions between platelet and collagen to inhibit aggregation (Bent *et al*., 2005).

Mill and Bone (2005) reported mild gastrointestinal complaints, headache, dizziness, allergic skin reactions and palpitations as possible side effects. Braun and Cohen (2010) also reported gastrointestinal upset, headache and dizziness including subarachnoid haemorrhage, subdural haematoma, intra-cerebral haemorrhage, sub-phrenic haematoma vitreous haemorrhage and postoperative bleeding as possible side effects of *Ginkgo*.

Literature suggests that *Ginkgo* is contraindicated prior to surgery, and with the use of anticoagulant drugs (Morgan, 2010) and to people with known sensitivity to *Ginkgo* preparations (Mills and Bone, 2005).

According to Bone (2007) the recommended dosing of Ginkgo biloba is 20 to 40 ml/week (2:1 liquid) or 6 to 12 g/day tablet.

The herb can be used during pregnancy, there are no adverse effects expected within recommended dosage in children and suspend treatment three days prior to surgery (Mediherb, 2006).

Panax ginseng

Panax ginseng is a nutritionally rich plant which is originally from China and Korea and capable of treating all kinds of illness thus known as the 'root of life'. It exerts a modifying or controlling influence on cognitive functions, electrical brain activity and peripheral blood glucose levels in healthy young people and increases secondary memory performance. It varies the strength of dealing with heavy load tasks on the memory aspect and attention processes and was found to have an effect on increasing the speed of thinking when dealing logically with certain facts that are known, dealing with numbers and with the view to arrive with the knowledge that is not known as yet (Reay *et al*., 2010).

Several studies found *Panax ginseng* to refine psychological function, exercise performance, immune function and conditions associated with diabetes; a study of 384 postmenopausal women who were randomised to receive placebo of *Ginseng* for 16 weeks showed improvement in their psychological general well-being index (Kiefer, 2003). A study of 20 young healthy volunteers showed improvement in cognitive performance, secondary memory performance, speed of performance memory tasks and accuracy of attention tasks (Kiefer, 2003).

Several studies report that *Ginseng* may improve performance on mental arithmetic, concentration, memory and slightly improve thinking or learning, but they have measured different kinds of mental function which makes it hard to know the exact effect of *Ginseng*. For example, a study showed that *Ginseng* increased the ability for abstract thought, but it

did not create any change in concentration levels, while in another study it was credited with helping the body deal with physical or mental stress (Ehrlich, 2005).
There is evidence that *Panax Ginseng* can improve quality of life; a study of 501 men and women living in Mexico City found better quality life measures (energy, sleep, sex life, personal satisfaction and wellbeing) when taking *Ginseng* (Ehrlich, 2005).

Panax ginseng is used to improve thinking, concentration, memory and work efficiency, physical stamina and athletic endurance and help an individual to cope with stress; it can serve as a stimulant to make people more active and feel calm (Kiefer, 2015)

Long term use of *Panax ginseng* may produce menstrual problems, breast pain, increased heart rate, high or low blood pressure, headache, loss of appetite, diarrhoea and vaginal bleeding (Ellis and Jewell, 2016) and high doses of *Ginseng* may cause mania, cerebral arteritis, oestrogenic effects and Stevens-Johnson syndrome (Mills and Bone, 2005).

Literature reports the following contraindications to *Panax ginseng*; concomitant use of pheneizine, acute infections, hypertension and hypertension in pregnancy (pre-eclampsia), pregnancy (except at lowest dose for a short period) and in adults with cardiac, hepatic and renal diseases (Morgan, 2012). According to Mill and Bone (2005) *Ginseng* should not be used by patients with acute asthma, signs of heat, excessive menstruation, nose bleeds, acute infections and hypertension.

According to Bone (2007) the recommended dosing of Panax ginseng is 7 to 40 ml/week (1:2 liquid) or 300 to 500mg/day tablet.
Safety precautions: The herb is safety to use during pregnancy and lactation, avoid concurrent use of stimulants and discontinue 3 days prior to anaesthesia (Mediherb, 2006).

Bacopa monerii

This is an aquatic (fresh water) plant that is mostly used in Ayurvedic traditional medicine of India to promote memory, longevity and intellectual functions. It has cholinergic, antioxidant and adoptogenic effects on the central nervous system. It improves audio-verbal and visual memory performance, verbal learning, and development of skills in

storing memory and improves retention in healthy older people (Morgan and Steven, 2010).

It has been shown to improve information processing speed and the rate of learning and lessened anxiety in healthy adults (Stough *et al*., 2001). Use of *Bacopa* shows improvement in motor functions, attention, language, memory, executive control, vision, emotions, sensory functions and consciousness. It was also concluded to have a potential in increasing the speed of attention in healthy and dementia patients (Kongkeaw *et al*. 2014).

A study that was conducted in Khon Kaen University in Thailand concluded that participants who were on Bacopa for 12 weeks scored far better in mental processing tests than those who were on placebo. A study at the University of Wollongong in Australia showed much improvement in memory and recall abilities of participants (Ravensthorpe, 2013).

It is also stated that *Bacopa* improves mood (depression, anxiety, stress and nervousness) by chemically supporting the effect of mood regulating neurotransmitters such as serotonin and acetylcholine and serves as a natural anti-depressant that does not have undesirable side effects. It improves the digestive system by supporting the production of mucus in the GIT and helps to absorb more important vitamins and minerals from food. In the respiratory system, *Bacopa* relaxes the bronchioles and blood vessels muscles around the airway passage to improve breathing (Ravensthorpe, 2013).

Bacopa has the potential to be a successful treatment for memory improvement in both healthy and aging adults, including those who suffer from age related memory impairment, and played a role in delaying memory decline or delaying Alzheimer's disease (Kairalla, 2011). This herbal substance was proven to decrease the rate of forgetting newly acquired information, during the study; tasks assessing attention, verbal and visual short-term memory and the retrieval of pre-experimental knowledge were not affected (Roodenrys et al. 2002).

Taking Bacopa on an empty stomach can cause gastrointestinal problems such as increased stool frequency, nausea, diarrhea, thirst or dry mouth and abdominal cramps. It may also cause muscle fatigue, decrease in felt stress and reduction in number of dreams

(Kongkeaw *et al*., 2014) and in some people it may produce weakness, loss of concentration, dizziness, irritation of the gastric mucus membranes and reflux however there are no known contraindications (Mills and Bone, 2005).

According to Bone (2007) the recommended dosing of Bacopa is 35 to 90 ml/week (1:2 liquid) 7.5 to 10.0 g/day tablet.

Safety precautions: use with caution during pregnancy and safe for use during lactation, use with caution in patient with pre-existing cholestasis. The use of herbs rich in saponins may be inadvisable in coeliac disease, fat malabsorption and some upper digestive irritation and topically to open wounds (Mediherb, 2006).

CHAPTER 3

MATERIALS AND METHODS

3.1 Recruitment

Recruitment of participants was conducted by advertising in the form of a research poster (approved by the Faculty of Health Sciences RHDC and the DUT IREC) that was displayed and disseminated on the DUT campuses (see Appendix A). Those who responded to the respective advertisements contacted the researcher directly who in turn booked their respective appointments at the DUT Homoeopathic Day Clinic.

3.2 Sampling

Since no sample frame was available on this population, non-probability sampling in the form of convenience sampling was applied whereby the first 30 (N=30) consenting respondents who meet the inclusion and exclusion criteria of the study will be recruited, the study recruited 31 participants which was desirable in the event of drop outs, of the 31 participants recruited 10 were randomly assigned to the placebo group and 21 to the treatment group.

3.3 Randomisation

A randomisation list was prepared by an independent clinician within the Department of Homoeopathy at DUT – Dr M. Maharaj. Thirty one pieces of paper each uniquely numbered from 1-31 were placed in a container, ten unique pieces of paper were then drawn from the container (each piece was replaced into the hat after being drawn) the first 10 numbers drawn comprised the placebo group (n=10) and the remaining 21 the treatment group (n=21) once the process was completed a randomisation list was compiled accordingly. The randomisation list remained blind to the researcher, research supervisor and the participants and was held securely by the independent clinician until the research was un-blinded – thus ensuring a double-blind methodology.

3.4 Selection of respondents

Prospective participants were required to meet certain pre-determined inclusion criteria and were excluded if they met certain exclusion criteria:

3.4.1 Inclusion criteria

Participants had to:

- be between 18 and 30 years of age
- be a registered tertiary education student
- be willing to follow the respective research process including 3 consultations with the researcher as well as comply with the research protocol and provide written informed consent
- be in a general good state of health
- have an ESS score of greater or equal to 10 [which suggested excessive sleepiness] (Johns 1991, Morrison and Riha 2012, Hayley *et al.* 2014) originating from inadequate sleep hygiene and insufficient sleep syndrome (Banerjee, Vitiello and Grunstein 2004, Hayley *et al.* 2014).

3.4.2 Exclusion criteria

Participants were not considered for inclusion if:

- they were younger than 18 or older than 30
- they were currently taking chronic or acute medication (orthodox, homoeopathic, herbal or other) for any medical condition
- they were using of any recreational drugs and drugs of abuse
- they suffered or had a history of narcolepsy, obstructive sleep disorder (apnoea), mood disorders or circadian rhythm disorders
- they were currently suffering from any chronic or debilitating disease
- they were night shift workers or had travelled internationally within the last 6 weeks
- they were commercial/occupational drivers, machine operators or pilots or had a history of sleep-associated incidents (Pagel 2009)
- they were pregnant, trying to conceive or breastfeeding

3.5 Informed consent

Informed consent was obtained from participants at two stages of the research; firstly, verbal (telephonic) informed consents were obtained from those who responded to the research advertisements according to APPENDIX A. Such verbal consents permitted the researcher to broadly screen prospective participants telephonically before booking their formal consultations and ensure that they met the basic inclusion criteria for the study.

The second stage of informed consent was in the form of a detailed information letter and face to face explanation of the research followed by written consent which was obtained from each prospective participant at the first formal consultation (APPENDIX B) at this stage all the requirements of the research participants were disclosed, and the research process was explained in detail, prospective participants were given details on the risks and benefits of participation and given opportunity to ask questions, once fully informed of the research process and willing to participant they signed an informed consent form and they were formally recruited into the study. Since the participants all attended a tertiary education institution of English medium all were familiar with English.

Participation was strictly voluntary and prospective participants were not coerced or incentivised in any manner in order to participate, furthermore they were free to withdraw from the study at any stage without giving any reason should they chose to do so.

The process of informed consent and the documentation applied was approved by the DUT Institutional Research Ethics Committee (IREC number: REC 72/16).

3.6 Consultations

3.6.1 First consultation

The following took place at the first consultation:

- Explanation of research procedure
- Informed consent process and signing of main informed consent form
- Confirmation that criteria for inclusion are met (Including ESS >10 Confirmation of diagnosis
- Physical examination and case history (See appendix E & F)
- Explanation of how to complete the Stanford Sleepiness Scale

3.6.2 Second consultation (a minimum of seven days after the first consultation)

The following took place at the second consultation:

- Handing in of seven days' baseline SSS by the patient – verification by researcher for correctness
- Completion of the baseline ESS (at the consultation)
- Dispensing of the experimental medication (placebo or active)
- Explanation of dosage and posology of medication
- Issuing of two further seven day SSS log sheets

3.6.3 Third consultation (a minimum of 14 days after the second consultation)

The following took place at the third consultation:

- Handing in of 2X seven days (14 days) SSS by the patient
- Completion of the final ESS (at the consultation)
- Retrieving of empty medicine containers
- Physical examination and case history
- Referral of participant for further care if necessary

3.7 Experimental medication

The individual herbal medicines were manufactured by Mediherb® a GMP and GLP (Good Laboratory Practice – Australia) compliant pharmaceutical manufacturer the products of which are supplied and distributed by COMED- Natura (South Africa).

3.7.1 Remedy manufacture

The experimental medicine was in the form of a herbal complex comprising the following pre-existing herbal medicines which were blended together in equal parts (the specific combination of ingredients was unique for this research) the herbal complex comprised:

Rhodiola rosea root (2:1 extract) *(*contains NLT 3.0 mg/mL rosavins and NLT 1.0 mg/mL salidroside) total percentage alcohol of extract = 45% ROH, Batch number: 16238.

Gingko Biloba leaf (2:1 extract) contains NLT 9.6 mg/mL ginkgo flavone glycosides total percentage alcohol of extract = 50% ROH, Batch number: 16609.

Panax Ginseng root (1:2 extract) (NLT 10.5 mg/mL ginsenosides with Rg_1:Rb_1 greater than or equal to 0.5 by HPLC) total percentage alcohol of extract = 60% ROH, Batch number: 16067 and 14081.

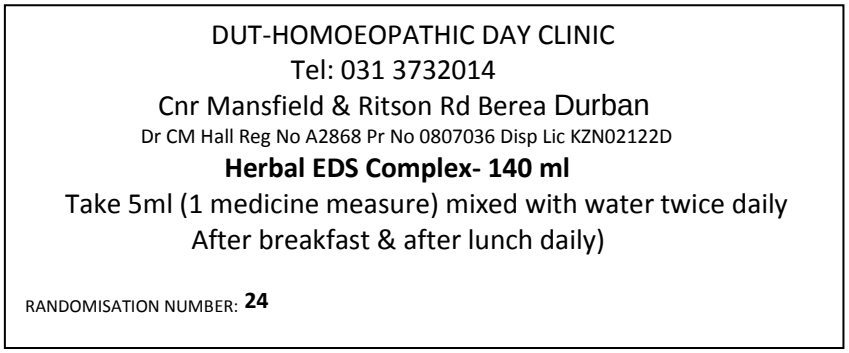
Bacopa monerii herb (1:2 Extract) total percentage alcohol of extract = 25% ROH, Batch number: 15075.

The research supervisor and research student blended the above ingredients together in equal parts at the Homoeopharmaceutics Laboratory at the DUT Homoeopathic Day Clinic and the final percentage alcohol was 45%.

The placebo comprised of a 20% ethanol and water solution.

Respective medicines i.e. herbal complex or alcohol placebo were dispensed by the laboratory technician and collected directly from clinic reception by the participants, the researcher thus did not see the medicine containers until such time as they were returned on completion of the study and data collection was over. Placebo or herbal complex were contained in amber glass bottles with indistinguishable labels as a further attempt to reduce identification, the researcher did not have the opportunity to inspect the bottles, taste or smell their content. Two additional placebo controlled EDS studies were conducted simultaneously with this one – in each study participants received 50ml amber glass bottles of homeopathic liquid or 20% ethanol placebo, the one study applied a homeopathic complex and the other a homoeopathic simillimum thus if participants discussed their medicines across studies the risk of distinguishing active vs placebo would have been difficult.

Figure 3.1 – Standardised label for medication



3.7.2 Dosage and posology

Each participant was provided with 140 ml of herbal complex (or placebo) in 150ml amber glass bottles and the dosage was prescribed as 5ml twice daily (mixed with water) i.e. since the herbal blend comprised equal parts of each ingredients participants effectively

received 2.5ml daily of each ingredient. The table below summarises the recommended dosages described by Bone (2007):

Herbal ingredient	**Recommended weekly dosage**
Rhodiola rosea	20-40ml/week (2.85 – 5.71ml per day)
Ginkgo biloba	20-40ml/week (2.85 – 5.71ml per day)
Panax ginseng	7-40ml/week (1-5.71ml per day)
Bacopa monerii	35-90ml/week (5-12.8ml per day)

3.8. Data collection

The two following tools were used to collect data:

3.8.1 Stanford Sleepiness Scale (SSS) (Hoddes *et al.* 1973)

The SSS was completed on a daily basis by each participant; for one week prior to commencing treatment followed by an additional two weeks of daily completion of the SSS (whilst on treatment). Participants rated their degree of sleepiness on an hourly basis throughout the awake period of the day using a seven point Guttmann scale (Bailes *et al.* 2006

Participants rated their degree of sleepiness in the following manner:

1 = Feeling active, vital, alert, or wide awake

2= Functioning at high levels, but not peak; able to concentrate

3= Awake, but relaxed; responsive but not fully alert

4= somewhat foggy, let down

5= Foggy; losing interest in remaining awake; slowed down

6= Sleepy, woozy, fighting sleep; prefer to lie down

7= No longer fighting sleep, sleep onset soon; having dream-like thoughts

X= Asleep

Participants chose the option which most suitably describes how they were feeling at the time of testing (Bailes *et al.* 2006). Scoring three or more during periods when one should be alert was suggestive of one experiencing sleep debt and more sleep was required.

3.8.2 Epworth Sleepiness Scale (ESS) (Johns 1991)

The ESS was applied at recruitment as one of the inclusion criterion, i.e. ESS score of 10 or above was required to qualify for the study, at the first consultation (pre-treatment baseline score) and again at the final consultation (post-treatment score).

Participants were asked how likely they were to fall asleep (in contrast to just feeling tired):

0= would never doze off

1= slight chance of dozing off

2= moderate change of dozing off

3= high chance of dozing off

In the following situations:

- Sitting and reading
- Watching TV
- Sitting inactive in a public place (e.g. theatre or meeting)
- As a passenger in a car for an hour without a break
- Lying down to rest in the afternoon when circumstances permit
- Sitting and talking to someone
- Sitting quietly after lunch without alcohol
- In a car, while stopped for a few minutes in the traffic

Once completed the scores were totalled and ranged from 0-24, the higher the score the higher the degree of sleepiness (Bailes *et al.* 2006)

3.9. Data analysis

Data from the ESS and SSS was entered into an Excel spread sheet and was analysed by an appointed statistician using the statistical software SPSS (version 24). Cross tabulation and bar graphs were used for descriptive statistics. Standard deviations and mean were used for numerical analysis.

The data was analysed using a combination of the following parametric tests:

3.9.1 Analysis of ESS data:

- Reliability testing and calculation of Cronbach alpha score which was used to provide a measure of the internal consistency (Tavakol and Dennick, 2011).
- The one sample Kolmogorov-Simrnov test: a nonparametric test of the equality of continuous, one dimensional probability distributions that was used to compare a sample with reference probability distributions (Taylor and John, 2011).
- Pearson's correlation: was used to measure the strength and direction of a linear relationship between two variables (Rumsey, 2016).
- Independent sample test: a test that compares means for two independent groups in cases of one variable (Brink *et al.,* 2008).
- ANOVA: the one-way analysis of variance was used to determine whether there are any statistically significant differences between the means (Turner and Thayer, 2001).

3.9.2 Analysis of SSS data:

According to Green and Salkind (2010), repeated measurements are collected in a longitudinal study, in which change over time is assessed. Repeated Factorial ANOVA was used in this study to tests for the main effects of time of treatment as well as the interaction of time of treatment for both treatment groups (Active and Placebo). According to Kinnear and Gray (2004), the analysis of variance of data from a factorial experiment offers tests not only for the presence of a main effect of each factor considered separately, but also for interactions between (or among) the factors. The effect of size of the treatment regime was also assessed using partial eta-squared. Kinnear and Gray (2004) had suggested that we consider a value less than 0.01 as a small effect, values between 0.01 to 0.10 as medium effect, and values greater than 0.10 as large effect. The afore-

mentioned parameters were considered when assessing the effect of size on respondent's ability to fall asleep.

3.10. Ethical considerations

The study met the requirements laid out in the Declaration of Helsinki (WMA 2013 and complied with the South African Department of Health Ethics in Health Research guidelines (DOH 2004). The study was granted ethical approval by the DUT Institutional Research Ethics Committee ethics number: REC72/16 summary ethical consideration was applied in the following broad categories.

- Participation was voluntary and free from coercion or undue incentive
- Participants were free to withdraw from the study at any stage without the need for providing a reason for their withdrawal
- Confidentiality was maintained i.e. all participant records were stored securely within a secure research storage facility within the Department of Homoeopathy, and ultimately shredded after 5 years. When data is disseminated participants were referred to by unique participant numbers and their respective identities will not be disclosed.
- Written informed consent was obtained from all participants prior to commencing the research project.
- Participants were autonomous and not considered to be a vulnerable population – all were English medium tertiary education students and thus there were no literacy or communication difficulties in obtaining informed consent.
- All risks to participation were carefully considered and based on this consideration the study is determined to be of 'minimal risk'.

CHAPTER 4

4.1 Introduction

This chapter presents the outcome of the data gathering process and reports on the results accordingly. In this section, the questionnaires (ESS and SSS) were the primary tools that were used to collect data and were distributed to 31 participants who were separated into two groups: group 1 was the active group (herbal complex) and group 2 was the placebo group. The data collected from the responses was analysed with SPSS (version 24®) in relation to the two objectives outlined in Chapter One, that is: (1) To determine the efficacy of a herbal complex in management of excessive daytime sleepiness in terms of ESS and (2) To determine the efficacy of a herbal complex in the management of excessive daytime sleepiness in terms of the SSS over 4 weeks of intervention.

All the data in the sections below were statistically analysed in an attempt to determine the efficacy of a herbal complex in the management of excessive daytime sleepiness in terms of ESS and SSS. The methods used in the study for ESS were:

1. Reliability testing and calculation of Cronbach alpha score which was used to provide a measure of the internal consistency (Tavakol and Dennick, 2011).
2. The one sample Kolmogorov-Simrnov test: a nonparametric test of the equality of continuous, one dimensional probability distributions that was used to compare a sample with reference probability distributions (Taylor and John, 2011).
3. Pearson's correlation: was used to measure the strength and direction of a linear relationship between two variables (Rumsey, 2016).
4. Independent sample test: a test that compares means for two independent groups in cases of one variable (Brink *et al,* 2008).
5. ANOVA: the one-way analysis of variance was used to determine whether there are any statistically significant differences between the means (Turner and Thayer, 2001).

The results were presented in descriptive format using bar graphs and cross tabulations and inferential techniques included the use of p-value, standard deviation, mean and standard error.

4.2 The sample

The research sample comprised 31 participants which were divided into two groups; a treatment (active) group (n = 21) and a placebo group (n = 10). The participants visited the Homeopathic clinic at the DUT and were randomly placed in the respective groups according to the methods described in 3.3

4.3 Biological data of participants

This section summarises the biographical characteristics of the participants which are described in terms of their gender and age distribution.

The entire sample was dominated by males 61.3%, females comprised 38.7% as seen in Table 4-1 the treatment/active group (n=21) comprised of 57.1% males and 42.9% females, and the placebo group (n=10) 70% male and 30% female. Overall, the Fischer exact test indicated that the proportion by gender between the two groups (active and placebo) was similar (p >0.05).

Table 4- 1: ***Gender distribution of participants***

			Group		Total
			Active	Placebo	
Gender	Male	Count	12	7	19
		% within Group	57.1%	70%	61.3%
	Female	Count	9	3	12
		% within Group	42.9%	30%	38.7%
Total		Count	21	10	31
		% within Group	100.0%	100.0%	100.0%

Fischer exact test score between groups (p = 0.697).

Table 4- 2: ***The descriptive statistics for age between groups***

Group	N	Mean	Std. Deviation	Maximum	Minimum
Active	19	21.48	2.40	25.00	19.00
Placebo	12	24.2	3.39	29.00	19.00
Total	31	22.3	2.99	29.00	19.00

Fischer exact test score between groups (p = 0.489).

As shown in Table 4-3, the placebo group had a slightly higher mean (24.2±3.39) age distribution when compared against the active group (21.48± 2.40). Importantly however the Fischer exact test revealed that there was no significant difference between the ages in both groups (p>0.05).

Overall, and as shown in Table 4-3, the female participants had the highest mean age distribution for the placebo (27±2.65) and male participants had the highest mean age distribution for the active group (21.5±2.47), respectively.

Table 4- 3: ***Gender by Age by Group***

Group	Gender	N	Mean	Std. Deviation	Maximum	Minimum
	Male	12	21.5	2.47	25.00	19.00
Active	Female	9	21.4	2.46	25.00	19.00
	Total	21	21.48	2.40	25.00	19.00
	Male	7	23.0	3.06	27.00	19.00
Placebo	Female	3	27.0	2.65	29.00	24.00
	Total	10	24.2	3.39	29.00	19.00
	Male	19	22.1	2.71	27.00	19.00
Total	Female	12	22.8	3.46	29.00	19.00
	Total	31	22.3	2.99	29.00	19.00

4.4 The Epworth Sleepiness Scale

The Epworth sleepiness scale is a subjective measure of a patient's degree of sleepiness that is widely used in the field of sleep medicine. Notably, the ESS test consists of eight situations in which patient's tendency to become sleepy is rated on a scale of 0, chance of dozing, to 3, high chance of dozing. (See 2.9.1)

4.4.1 Reliability of the ESS

Before discussing the findings of this study, this section deliberately focuses on a few issues of reliability. Reliability is computed by taking several measurements on the same subjects. A reliability coefficient of 0.70 or higher is considered as "acceptable". The table below reflects the Cronbach's alpha score for all the items that constituted the ESS questionnaire.

As shown in Table 4-4, the reliability scores for the active group were slightly less than the acceptable score of 0.70 the other 2 reliability scores exceed the recommended value. This indicates a degree of consistency for this section of the questionnaire. It is also important to note that the reliability score for the total research sample (combined active and placebo groups) significantly exceeded the benchmark of 0.70.

Table 4- 4: ***Survey scales and Predictor variables in Quantitative Analysis***

Survey scales	Predictor variables	Number of Items	Cronbach's Alpha score
1	Active	8	0.564
2	Placebo	8	0.896
3	Combined	8	0.777

4.4.2 Analysis of ESS data – section analysis

The section that follows analyses the scoring patterns of the participants per variable per section. The results are first presented using summarised percentages for the variables that constitute each section. Results are then further analysed according to the importance of the statements. The traditional approach to reporting a result requires a statement of statistical significance. A **p-value** is generated from a **test statistic.** A significant result is indicated with "$p < 0.05$".

Each question within the ESS was numbered from 1-8 and analysed individually and compared between groups at the three intervals of measurement.

The table 4- 5 below indicates the relationship between the two groups by individual reading.

Table 4- 5: ***Participants ratings of their sleepiness using the ESS***

	Group								
	Active				Placebo				
	Never	Slight	Moderate	High	Never	Slight	Moderate	High	Fisher's Exact Test
ESS_1_1	5.3%	10.5%	42.1%	42.1%	8.3%	16.7%	58.3%	16.7%	0.536
ESS_1_2	15.8%	26.3%	36.8%	21.1%	8.3%	33.3%	33.3%	25.0%	1.000
ESS_1_3	15.8%	31.6%	42.1%	10.5%	16.7%	0.0%	50.0%	33.3%	0.120
ESS_1_4	5.3%	21.1%	42.1%	31.6%	0.0%	8.3%	41.7%	50.0%	0.682
ESS_1_5	10.5%	10.5%	26.3%	52.6%	0.0%	8.3%	25.0%	66.7%	0.869
ESS_1_6	31.6%	42.1%	26.3%	0.0%	58.3%	16.7%	16.7%	8.3%	0.175
ESS_1_7	10.5%	42.1%	26.3%	21.%	16.7%	33.3%	25.0%	25.0%	0.956
ESS_1_8	36.8%	26.3%	21.1%	15.8%	25.0%	50.0%	25.0%	0.0%	0.370
ESS_2_1	0.0%	26.3%	42.1%	31.6%	0.0%	25.0%	41.7%	33.3%	1.000
ESS_2_2	15.8%	15.8%	36.8%	31.6%	16.7%	16.7%	25.0%	41.7%	0.951
ESS_2_3	10.5%	57.9%	21.1%	10.5%	33.3%	25.0%	8.3%	33.3%	0.101
ESS_2_4	15.8%	15.8%	15.8%	52.6%	0.0%	8.3%	41.7%	50.0%	0.320
ESS_2_5	0.0%	5.3%	21.1%	73.7%	0.0%	0.0%	25.0%	75.0%	1.000
ESS_2_6	26.3%	42.1%	26.3%	5.3%	33.3%	58.3%	0.0%	8.3%	0.265
ESS_2_7	10.5%	21.1%	42.1%	26.3%	16.7%	16.7%	33.3%	33.3%	0.915
ESS_2_8	36.8%	21.1%	36.8%	5.3%	16.7%	50.0%	33.3%	0.0%	0.303
ESS_3_1	21.1%	21.1%	36.8%	21.1%	33.3%	41.7%	16.7%	8.3%	0.395
ESS_3_2	31.6%	26.3%	31.6%	10.5%	33.3%	16.7%	41.7%	8.3%	0.948
ESS_3_3	47.4%	31.6%	21.1%	0.0%	33.3%	41.7%	16.7%	8.3%	0.684
ESS_3_4	31.6%	36.8%	15.8%	15.8%	8.3%	50.0%	25.0%	16.7%	0.523
ESS_3_5	21.1%	15.8%	36.8%	26.3%	0.0%	25.0%	33.3%	41.7%	0.392
ESS_3_6	57.9%	26.3%	10.5%	5.3%	66.7%	25.0%	0.0%	8.3%	0.920
ESS_3_7	21.1%	47.4%	21.1%	10.5%	33.3%	25.0%	25.0%	16.7%	0.637
ESS_3_8	42.1%	36.8%	15.8%	5.3%	25.0%	58.3%	8.3%	8.3%	0.633

The Fisher's exact tests individual readings for the degree of sleepiness is summarised in the table above. As indicated by the level of significance, it was noted that there were no statistically significant differences between the active and the placebo in all of the individual readings of the ESS (p>0.05).

From the above findings, it can be gathered that the treatment had little significant impact on the sleepiness of the participants, overall. Notwithstanding this, it was

observed that there was a slight improvement in the participant's degree of sleepiness after the third visit. For instance, at the first visit (ESS_1_1), participants were asked to rate their degree of sleepiness while sitting and reading. 42.1% of the participants in the active group indicated that they had high chance of falling asleep while sitting and reading, whereas 31.6% of the active group participants reported similar chance of falling asleep after the second visit. Notably, it can be observed that only 21.1% of these active group participants in the third visit indicated falling asleep while sitting and reading; suggesting a reduction in propensity to fall asleep in this setting. Similar trends could be observed for the placebo group for the second and third visit, respectively.

With regard to the participant rating of their degree of sleepiness when watching television, 21.1% of the participants in the active group reported they had high chance of falling asleep in the first visit (ESS_1_2). The tendency to fall asleep, however, increases to 31.6% in the second visit (ESS_2_2). In contrast, and in the third visit (ESS_3_2), only 8.3% of them indicated they had high chance of falling asleep while watching television; suggesting a reduction in tendency to fall asleep in this setting. Similar trends could be observed for the placebo group.

Regarding the participant rating of their degree of sleepiness when lying down to rest in the afternoon when circumstances permit, 52.6% of the participant in the active group indicated they had high chance of falling asleep during their first visit (ESS_1_5). In the second visit (ESS_2_5), for example, it can be observed that the participant chances to fall asleep had increased to 73.7%. These chances, however, decrease to 26.3% after the third visit (ESS_3_5); suggesting a reduction in tendency to fall asleep in this setting. Similar trends could be observed for the placebo group.

4.4.3 ESS Comparison of means

To determine whether parametric tests could be used, a One-Sample Kolmogorov-Smirnov Test was done. The normal distribution of the degree of sleepiness is presented in the table below. The One-Sample Kolmogorov-Smirnov test for the normality revealed no significant differences against the normality of the variables (p>

0.05). Hence it can be inferred that the distributions are normal and that the t-test and ANOVA can be used to analyse the respective data set.

Table 4- 6: ***Normal Distribution Test***

		ESS - Total 1	ESS - Total 2	ESS - Total 3
N		31	31	31
Normal Parameters	Mean	13.4839	14.1613	9.2903
	Std. Deviation	3.02072	3.19475	4.53280
Most Extreme Differences	Absolute	.204	.123	.147
	Positive	.204	.123	.147
	Negative	-.124	-.093	-.089
Test Statistic		.204	.123	.147
Asymp. Sig. (2-tailed)		.095	.200	.084

4.4.4. ESS Intra-group analysis of placebo group

The intra-group relationship of the participant's individual scores within the placebo group is explained in this section.

With regards to the Placebo group and as indicated by the level of significance in the table above, it is noted that there was a strong correlation (r=0.838; 0.712, $p< 0.05$) between the three pairs of scores. Significantly, an examination of the means indicates that the means are similar for readings for the first and second visit, but lower for reading third visit. The lower mean (9.7±4.96) measured in the third visit (ESS=Total 3) suggests that the placebo had some positive effect on the sleepiness, as treatment administration commenced after the second visit and the measurement at the third visit was the post-intervention score.

Table 4- 7: ***ESS Intra-group analysis of Placebo group***

		ESS - Total 1	ESS - Total 2	ESS - Total 3
ESS - Total 1	Pearson Correlation	1		
	Sig. (2-tailed)			
	N	12		
ESS - Total 2	Pearson Correlation	.838**	1	
	Sig. (2-tailed)	.001		
	N	12	12	
ESS - Total 3	Pearson Correlation	.712**	.813**	1
	Sig. (2-tailed)	.009	.001	
	N	12	12	12

**. Correlation is significant at the 0.01 level (2-tailed).

Table 4- 8: ***Descriptive Statistics for ESS Intra-group analysis of Placebo group***

	N	Minimum	Maximum	Mean	Std. Deviation
ESS - Total 1	12	10.00	23.00	13.9167	3.82476
ESS - Total 2	12	8.00	23.00	14.4167	4.20948
ESS - Total 3	12	4.00	23.00	9.6667	4.96045

Table 4- 9: ***Independent Paired Samples Test for Placebo***

		Paired Differences					t	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	ESS - Total 1 - ESS - Total 2	-.50000	2.31595	.66856	-1.97149	.97149	-.748	11	.470
Pair 2	ESS - Total 1 - ESS - Total 3	4.25000	3.49350	1.00849	2.03034	6.46966	4.214	11	.001*
Pair 3	ESS - Total 2 - ESS - Total 3	4.75000	2.89592	.83598	2.91002	6.58998	5.682	11	.000*

The independent t-test, mean, standard deviation, and standard error results for the intra group analysis of the placebo group are illustrated in Table 4-9. Significant differences were found in the baseline results compared to the latter time periods ($p < 0.05$) i.e. when comparing ESS total score 1 (at recruitment) with ESS total score 3 (post-treatment) and ESS total score 2 (at baseline) and ESS total score 3 (post-treatment). No significant differences were found between ESS-Total 1 (first visit) and ESS-Total 2 (second visit) this is expected as the intervention was only applied after the second ESS score. Such data is suggestive of the placebo intervention resulting in a statistically significant reduction in ESS scores i.e. participants were less sleepy.

4.4.5. ESS Intra-group analysis of the active group

The intra-group relationship of the participant's individual scores within the Active group is explained in this section.

With reference to the Active group and as indicated by the level of significance in the table above, it is noted that there is only one significant result (r=0.584; $p< 0.05$) between the first and second readings. An examination of the means indicates that the means are similar for readings for the first and second visit, but lower for reading third visit. The lower mean (9.1±4.36) measured in the third visit (ESS=Total 3) suggests that the Active treatment had positive effect on the sleepiness as treatment administration commenced after the second visit and the measurement at the third visit was the post-intervention score. The table below indicates the correlations for the active group.

Table 4- 10: ***ESS Intra-group analysis of Active group***

		ESS - Total 1	ESS - Total 2	ESS - Total 3
ESS - Total 1	Pearson Correlation	1		
	Sig. (2-tailed)			
	N	19		
ESS - Total 2	Pearson Correlation	.584**	1	
	Sig. (2-tailed)	.009		
	N	19	19	
ESS - Total 3	Pearson Correlation	.381	.031	1
	Sig. (2-tailed)	.107	.900	
	N	19	19	19

**. Correlation is significant at the 0.01 level (2-tailed).

Table 4- 11: ***Descriptive Statistics for ESS Intra-group analysis of Active group***

	N	Minimum	Maximum	Mean	Std. Deviation
ESS - Total 1	19	10.00	20.00	13.2105	2.46259
ESS - Total 2	19	10.00	17.00	14.0000	2.47207
ESS - Total 3	19	.00	17.00	9.0526	4.36493

The independent t-test, mean, standard deviation, and standard error results for the intra group Active Group are shown in Table 4-11. Significant differences were found in the baseline results compared to the latter time periods ($p < 0.05$) i.e. when comparing ESS total score 1 (at recruitment) with ESS total score 3 (post-treatment) and ESS total score 2 (at baseline) and ESS total score 3 (post-treatment). No significant differences were found between ESS-Total 1 (first visit) and ESS-Total 2 (second visit) ($p>0.05$). This is expected as the intervention was only applied after the second ESS score. There was a statistically significant improvement in ESS-Total 3 scores (a lowering in total ESS score) in participants of the Active Group suggesting that they were significantly less sleepy by the end of the third visit (post-treatment)

Table 4-12 further illustrates the differences in the mean values of ESS sleepiness value obtained through the various participant visiting periods. It is observed that the readings at time period three visit were lower than that of the other time periods.

Table 4- 12: ***Independent Paired Samples Test for Active Group***

		Paired Differences					T	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	ESS - Total 1 - ESS - Total 2	-.78947	2.25041	.51628	-1.87413	.29519	-1.529	18	.144
Pair 2	ESS - Total 1 - ESS - Total 3	4.15789	4.11317	.94362	2.17541	6.14038	4.406	18	.000*
Pair 3	ESS - Total 2 - ESS - Total 3	4.94737	4.94945	1.13548	2.56181	7.33293	4.357	18	.000*

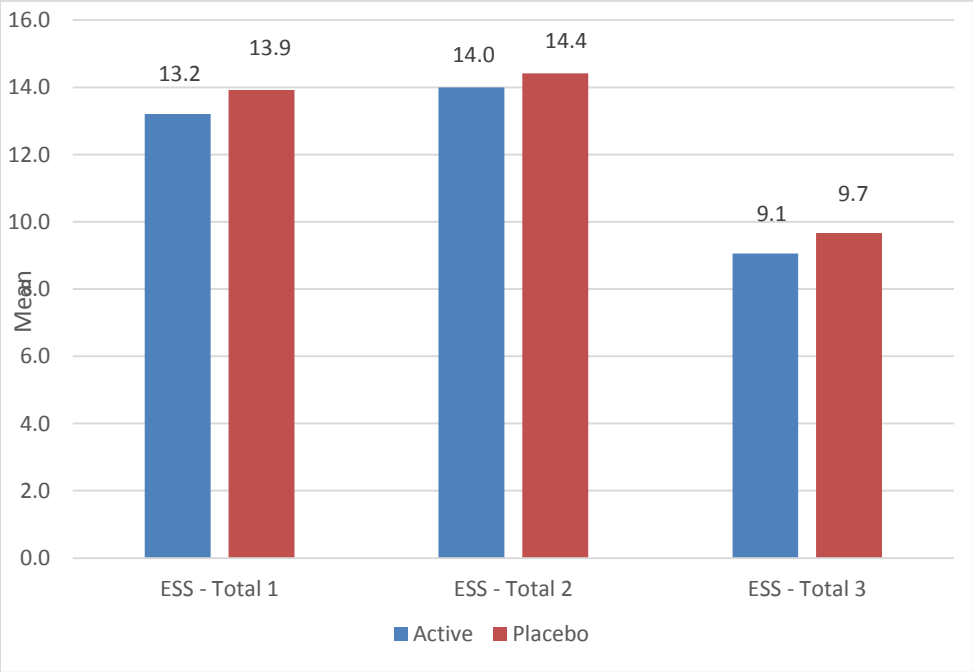


*Figure 4- 1****: Comparison of mean ESS total scores between groups***

4.4.6 ESS INTER-GROUP ANALYSIS

The inter-group relationship of the participants' individual readings for both the Placebo and Active Groups is explained in this section.

As shown in Table 4-13, it was noticed that none of the p-values were significantly different between groups. That is, there were no statistically significant differences between the two groups at each interval (p> 0.05). Overall however the mean ESS values measured in the Active group were consistently lower than the Placebo group (Table 4-14).

Additionally, and in respect to the participants rating of their degree of sleep sufficiency after receiving both Active and Placebo treatment, it can be gleaned from Figure 4-2 difference in the participant's ratings. After the third visit (ESS-3), for example, 31.5% of the participant in the Active Group had ESS scores suggestive of sufficient degree of alertness, whereas within the Placebo Group at ESS-3 only 25% had ESS scores suggestive of sufficient alertness. It can therefore be inferred that the active treatment was effective in reducing the tendency of the participants to fall asleep.

Table 4- 13: ***Inter-group ANOVA results for both Active and Placebo groups***

		Sum of Squares	df	Mean Square	F	Sig.
ESS - Total 1 * Group	Between Groups (Combined)	3.667	1	3.667	.394	.535
	Within Groups	270.075	29	9.313		
	Total	273.742	30			
ESS - Total 2 * Group	Between Groups (Combined)	1.277	1	1.277	.121	.730
	Within Groups	304.917	29	10.514		
	Total	306.194	30			
ESS - Total 3 * Group	Between Groups (Combined)	2.773	1	2.773	.131	.720
	Within Groups	613.614	29	21.159		
	Total	616.387	30			

Table 4- 14: ***Mean, Standard deviation, minimum, and range for both Active and Placebo Groups***

Group		ESS - Total 1	ESS - Total 2	ESS - Total 3
Active	N	19	19	19
	Mean	13.2105	14.0000	9.0526
	Std. Deviation	2.46259	2.47207	4.36493
	Maximum	20.00	17.00	17.00
	Minimum	10.00	10.00	.00
Placebo	N	12	12	12
	Mean	13.9167	14.4167	9.6667
	Std. Deviation	3.82476	4.20948	4.96045
	Maximum	23.00	23.00	23.00
	Minimum	10.00	8.00	4.00

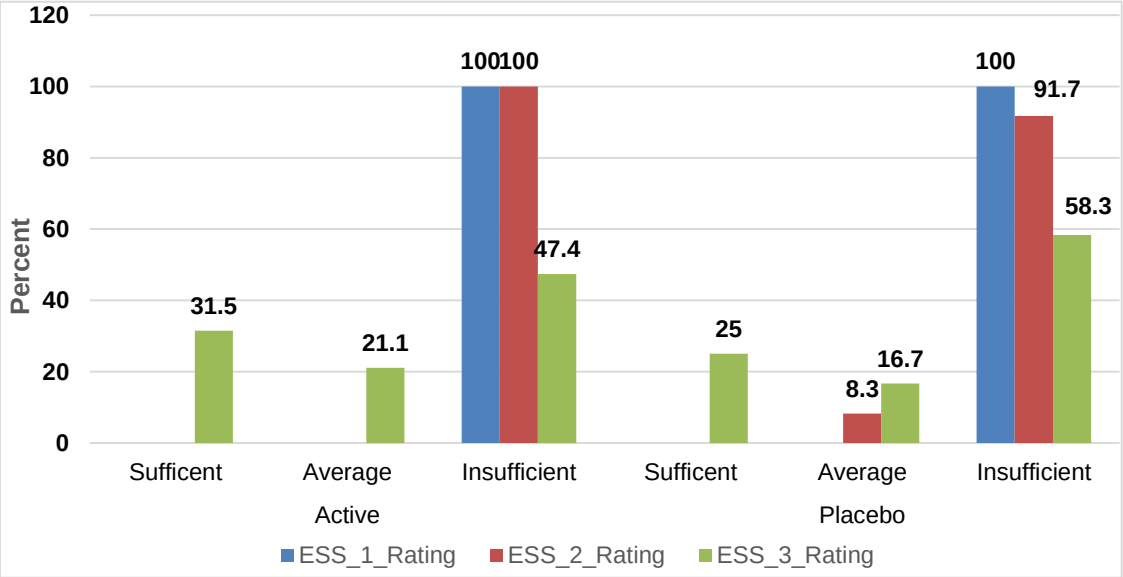


*Figure 4- 2****: Comparison degree of alertness based on ESS scores between groups***

4.5 Stanford Sleepiness Scale (SSS)

The Stanford sleepiness scale is a quick and easy way to assess how alert you are feeling. Using a 7-point scale, the SSS used introspectively to measure the degree of sleepiness of the participant. (See 2.9.2).

This section uses a mixed factorial ANOVA to test the difference across time (hours) in the SSS scores that were assessed between 7am-7pm (daytime hours) for three weeks. Specifically, attempt to evaluate the effect of time (hours) on the participant's ability to fall asleep. Subsequently, a comparison by weeks on the total number of symptoms experienced in a week was tested in order to evaluate the effectiveness of the treatment regime in reducing sleepiness.

4.5.1 Mauchly's Test of Sphericity by Hours

Table 4-15 showed the test for sphericity for the participant's rating of their sleepiness. The Mauchly test has a p-value of 0.000, which suggests evidence of heterogeneity of covariance of the responses. It suggested that lower Huynh-Feldt be used with smaller departures from sphericity, while Greenhouse-Geisser is used when the departures are large. The greenhouse-Geisser adjustment of the ANOVA (F) test was therefore used in assessing the sleepiness on the SSS

*Table 4- 15**: Mauchly's test of Sphericity by hours***

Mauchly's Test of Sphericity[a]							
Measure:							
Within Subjects Effect	Mauchly's W	Approx. Chi-Square	Df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Time	0	188.038	77	0.000	0.23	0.33	0.083

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Group

Within Subjects Design: Time

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

4.5.2 SSS assessment for week 1 (Pre-treatment)

4.5.2.1 Descriptive Statistics for Week 1

Table 4-16 showed the participants rating of the SSS by hour for the first week of assessment. It can be gathered from the table below that 7am had the highest ability to induce sleep for both the Active and Placebo. This tendency was observed to be lowest at 10am for the Active group and 11 am for the placebo, respectively

*Table 4- 16**: Respondents rating of the SSS for week one***

Treatment group		Mean	Std. Deviation	N
	Active	5.81	0.49716	7
7AM	Placebo	5.7143	0.80297	7
	Total	5.7621	0.64353	14
	Active	4.6743	0.44056	7
8AM	Placebo	4.2571	0.76997	7
	Total	4.4657	0.64036	14
	Active	3.2043	0.42075	7
9AM	Placebo	3.2143	0.87069	7
	Total	3.2093	0.65698	14
	Active	2.62	0.19698	7
10AM	Placebo	2.4714	0.66009	7
	Total	2.5457	0.47429	14
	Active	2.6129	0.25474	7
11AM	Placebo	2.0429	0.59121	7
	Total	2.3279	0.52796	14
	Active	2.6943	0.26776	7
12AM	Placebo	2.5714	1.02748	7
	Total	2.6329	0.72416	14
	Active	3.0057	0.32944	7
1PM	Placebo	3.1571	1.0374	7
	Total	3.0814	0.74362	14
	Active	3.3	0.25962	7
2PM	Placebo	3.6	0.80208	7
	Total	3.45	0.59352	14

	Active	3.4157	0.36345	7
3PM	Placebo	3.5714	0.54685	7
	Total	3.4936	0.45334	14
	Active	3.6471	0.25545	7
4PM	Placebo	3.4286	0.51547	7
	Total	3.5379	0.40696	14
	Active	3.79	0.27068	7
5PM	Placebo	4.2857	0.6283	7
	Total	4.0379	0.5312	14
	Active	3.7614	0.34329	7
6PM	Placebo	3.9857	0.89336	7
	Total	3.8736	0.66052	14
	Active	3.3457	0.2741	7
7PM	Placebo	4.3714	0.84797	7
	Total	3.8586	0.8061	14

4.5.2.2 ANOVA Tests of Within-Subjects and Between Effects for Week 1

As shown in Table 4-17, the mean sleepiness scores for the Active and Placebo group with respect time differed significantly beyond the 0.001 level: F (2.756,33.071) = 33.991; p< 0.000(with Greenhouse-Geisser adjustment). Partial eta squared = 0.739 representing a large effect. There was no significant interaction between groups and time: F (2.756, 33.071) = 1.79; p > 0.05 (with Greenhouse-Geisser adjustment). Partial eta squared =0.127 representing a large effect.

*Table 4- 17**: Tests of Within-Subjects Effects Week 1***

Source		Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Time	Greenhouse-Geisser	138.056	2.756	50.095	33.991	0.000	0.739
Time * Group	Greenhouse-Geisser	7.106	2.756	2.579	1.75	0.179	0.127
Error(Time)	Greenhouse-Geisser	48.739	33.071	1.474			

As shown in Table 4-18, the mean scores for the treatment groups of the respondent rating of the SSS showed no significant differences beyond 0.01 level: F (1, 12) = 0.25; p >0.05. Partial eta squared = 0.02 representing a medium effect.

*Table 4- 18**: Test of Between-Subjects Effects Week 1***

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	2306.239	1	2306.239	3434.591	0.000	0.997
Group	0.168	1	0.168	0.25	0.626	0.02
Error	8.058	12	0.671			

Although the mean score for the Active group sleepiness (3.529) was slightly lower than the Placebo (3.590), a Bonferroni test (table 4-19) failed to show significance in the respondents ability to fall asleep (p> 0.05). This suggests that the tendency to fall asleep was the same for both Active and Placebo group prior to commencing treatment i.e. the respective groups were statistically similar at the outset of the study

*Table 4- 19**: Bonferroni-Pairwise Comparison between treatments groups Week1***

(I) Treatment group	Mean	Mean Difference (I-J)	Std. Error	Sig.[a]	95% Confidence Interval for Difference [a]	
					Lower Bound	Upper Bound
Active	3.529	-0.061	0.121	0.626	-0.325	0.204
Placebo	3.590					

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

Figure 4-3 further confirms the pattern of the sleepiness by hour for the first week of assessment. It can be gleaned that after 4 hours, the tendencies of the participants to fall asleep greatly reduces. Subsequently, their sleepiness tendency increases thereafter for the next five hours, for both the Active and Placebo group. Interestingly, the Active group experience a gradual reduction of sleepiness after 12 hours.

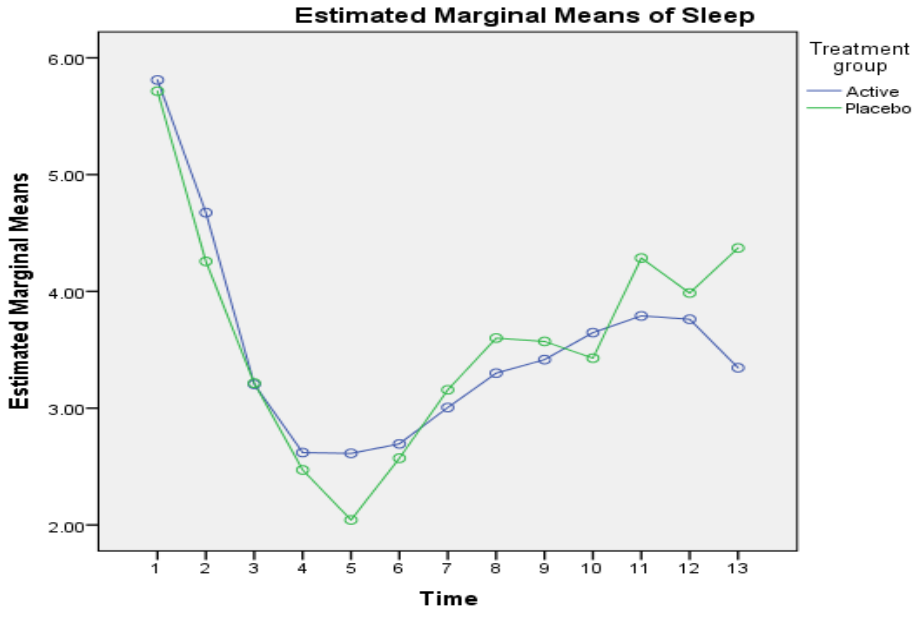


*Figure 4- 3**: Differences in the mean scores estimate at week 1***

4.5.3 SSS Assessment for Week 2 (1-week post treatment)

4.5.3.1 Descriptive Statistics for Week 2

Table 4-20 showed the participants rating of the SSS by hour for the second week of assessment. It can be gathered from the table below that 7am had the highest ability to induce sleep for both the Active and Placebo (no change from baseline week). This tendency was observed to be lowest at 10am for the Active group and 12 pm for the placebo, respectively for the second week of assessment.

*Table 4- 20**: Respondents rating of the SSS for week 2***

	Treatment group	Mean	Std. Deviation	N
7AM	Active	4.8371	0.40265	7
	Placebo	6.1714	0.80149	7
	Total	5.5043	0.92229	14
8AM	Active	3.3671	0.64644	7
	Placebo	4.8	0.8124	7
	Total	4.0836	1.02481	14
9AM	Active	2.8343	0.27214	7
	Placebo	4.1143	0.85524	7
	Total	3.4743	0.90159	14
10AM	Active	2.3271	0.25151	7
	Placebo	3.0571	0.46853	7
	Total	2.6921	0.52344	14
11AM	Active	2.3729	0.30598	7
	Placebo	2.5714	0.45356	7
	Total	2.4721	0.38571	14

	Active	2.6857	0.28867	7
12PM	Placebo	2.4857	0.38483	7
	Total	2.5857	0.3429	14
	Active	2.7557	0.37425	7
1PM	Placebo	2.9714	0.58797	7
	Total	2.8636	0.48655	14
	Active	3.0614	0.25373	7
2PM	Placebo	3.4857	0.50803	7
	Total	3.2736	0.44419	14
	Active	3.0414	0.49097	7
3PM	Placebo	3.4857	0.50803	7
	Total	3.2636	0.53246	14
	Active	3.1971	0.57174	7
4PM	Placebo	3.7857	0.72899	7
	Total	3.4914	0.69958	14
	Active	3.3529	0.56797	7
5PM	Placebo	3.3143	0.65683	7
	Total	3.3336	0.59026	14
	Active	3.1443	0.50947	7
6PM	Placebo	3.1	0.68557	7
	Total	3.1221	0.58073	14
	Active	3.1986	0.41807	7
7PM	Placebo	3.5571	0.65027	7
	Total	3.3779	0.55718	14

4.5.3.2 ANOVA Tests of Within-Subjects and Between Effects for Week 2

As shown in Table 4-21, the mean sleepiness scores for the Active and Placebo group with respect of time for the second week differed significantly beyond the 0.001 level: F (3.87546.503) = 30.947; p < 0.001 (with Greenhouse-Geisser adjustment). Partial eta squared = 0.721 representing a large effect. This suggests that the tendency to fall asleep for the Active and Placebo group was not the same for week two i.e. the groups differed in this respect statistically. More so, there were significant interaction between groups and time: F (3.875, 46.503) = 3.716; p < 0.05. Partial eta squared =0.236 representing a large effect. This indicates that the sleepiness pattern that is the tendency to fall asleep changes with time with a large effect.

*Table 4- 21**: Tests of Within-Subjects Effects Week 2***

Source		Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Time	Greenhouse-Geisser	102.269	3.875	26.39	30.947	0.000	0.721
Time * Group	Greenhouse-Geisser	12.279	3.875	3.169	3.716	0.011	0.236
Error(Time)	Greenhouse-Geisser	39.656	46.503	0.853			

As shown in Table 4-22, the mean scores for the treatment groups of the participants rating of the SSS showed significant differences beyond 0.01 level: F (1, 12) = 21.376; p < 0.01. Partial eta squared = 0.64 representing a large effect. This indicates that the tendency to fall asleep for the second week was significantly different between the Active and Placebo group.

*Table 4- 22**: Test of Between-Subjects Effects Week 2***

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	2041.356	1	2041.356	3584.44	0	0.997
Group	12.174	1	12.174	21.376	0.001	0.64
Error	6.834	12	0.57			

Table 4-23 showed the pair wise comparison by treatment for week two. The mean response of sleepiness for the Active group (3.090) was lower than the mean of the placebo (3.608). A Bonferroni test confirmed that the Active group was significantly less sleepy than the Placebo for the second week two of treatment (p <0.01).

*Table 4- 23**: Bonferroni-Pairwise Comparison between treatments groups Week 2***

(I) Treatment group	Mean	Mean Difference (I-J)	Std. Error	Sig.[a]	95% Confidence Interval for Difference[a]	
					Lower Bound	Upper Bound
Active	3.090	.517	0.112	0.001	0.273	0.761
Placebo	3.608					

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Figure 4-4 shows the pattern of the sleepiness by hour for the second week of assessment. It was observed that the sleepiness rapidly reduced for the first 3hours for the Active and 4hours for the Placebo. More so, it can be seen that there was a slow

increase in the tendency to fall asleep for the Active group, whilst the Placebo experience higher degree of sleepiness for the same period.

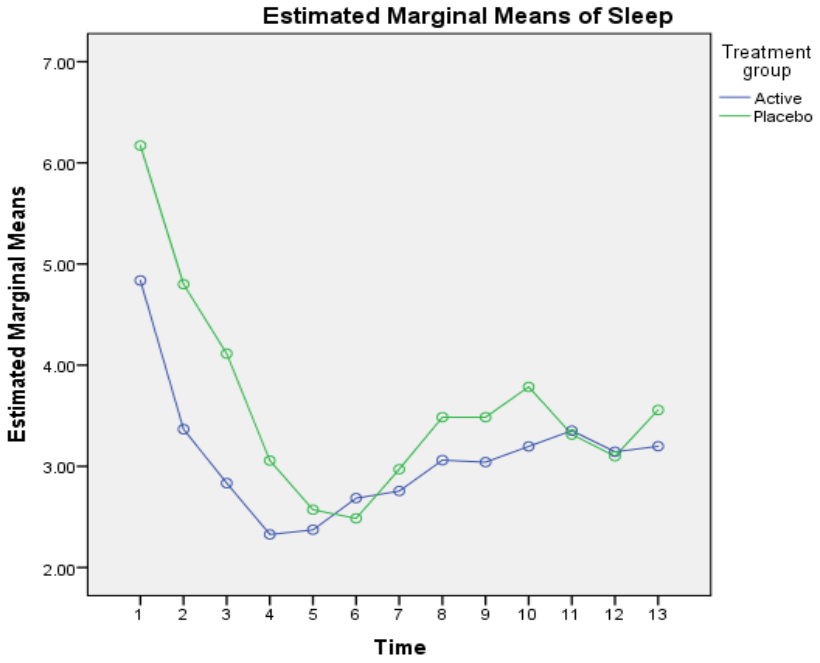


*Figure 4- 4**: Differences in the mean scores estimate at week 2***

4.5.4 SSS Assessment for Week 3 (2-weeks post treatment)

4.5.4.1 Descriptive Statistics for Week 3

Table 4-24 showed the participants rating of the SSS by hour for the third week of assessment. It can be observed from the table below that 7am had the highest ability to induce sleep for both the Active and Placebo (unchanged from baseline). This tendency was observed to be lowest at 11am for the Active group and 1 pm for the placebo, respectively for the second week of assessment.

*Table 4- 24**: Respondents rating of the SSS for week 3***

Treatment groups		Mean	Std. Deviation	N
	Active	3.4414	0.40081	7
7AM	Placebo	6.4429	0.43916	7
	Total	4.9421	1.60889	14
	Active	2.7271	0.56249	7
8AM	Placebo	4.6143	0.50143	7
	Total	3.6707	1.10494	14
	Active	2.3329	0.48152	7
9AM	Placebo	3.2429	0.46496	7
	Total	2.7879	0.65555	14
	Active	2.0829	0.34587	7
10AM	Placebo	2.6286	0.55891	7
	Total	2.3557	0.52874	14
	Active	1.9657	0.18073	7
11AM	Placebo	2.5286	0.55291	7
	Total	2.2471	0.49139	14
	Active	2.0214	0.24361	7
12PM	Placebo	2.2857	0.49809	7
	Total	2.1536	0.40088	14
	Active	2.4271	0.33185	7
1PM	Placebo	2.0286	0.43861	7
	Total	2.2279	0.42707	14
	Active	2.3014	0.27751	7
2PM	Placebo	2.1429	0.58269	7
	Total	2.2221	0.44611	14
3PM	Active	2.5286	0.23112	7

	Placebo	2.3286	0.46445	7
	Total	2.4286	0.3674	14
	Active	2.7214	0.28399	7
4PM	Placebo	2.5714	0.4348	7
	Total	2.6464	0.36129	14
	Active	2.7014	0.4348	7
5PM	Placebo	2.7571	0.54423	7
	Total	2.7293	0.47412	14
	Active	2.8743	0.54347	7
6PM	Placebo	2.8286	0.43095	7
	Total	2.8514	0.4718	14
	Active	2.7157	0.35758	7
7PM	Placebo	3.3	0.7303	7
	Total	3.0079	0.63014	14

4.5.4.2 ANOVA Tests of Within-Subjects and Between Effects for Week 3

As shown in Table 4-25, the mean sleepiness scores for the Active and Placebo group with respect of time differed significantly beyond the 0.001 level: $F(4.173,50.078) = 43.634$; $p < 0.001$ (with Greenhouse-Geisser adjustment). Partial eta squared = 0.784 representing a large effect. This suggests that the tendency to fall asleep for the Active and Placebo group was not the same for week three i.e. the groups differed in this respect statistically. In addition, there was also significant interaction between groups and time: $F(4.173, 50.078) = 16.892$; $p < 0.001$ (with Greenhouse-Geisser adjustment). Partial eta squared =0.585 representing a large effect. This indicates that the sleepiness pattern that is the tendency to fall asleep changes with time with a large effect.

*Table 4- 25**: Tests of Within-Subjects Effects Week 3***

Source		Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Time	Greenhouse-Geisser	99.965	4.173	23.954	43.634	0.000	0.784
Time * Group	Greenhouse-Geisser	38.700	4.173	9.274	16.892	0.000	0.585
Error(Time)	Greenhouse-Geisser	27.492	50.078	0.549			

As shown in Table 4-26, the mean scores for the treatment groups of the participants rating of the SSS showed significant differences beyond 0.001 level: F (1, 12) = 33.743; $p < 0.001$. Partial eta squared = 0.738 representing a large effect. This indicates that the tendency to fall asleep for the third week was significantly different between the Active and Placebo group.

*Table 4- 26**: Test of Between-Subjects Effects Week 3***

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	1416.762	1	1416.762	3774.774	0.000	0.997
Group	12.665	1	12.665	33.743	0.000	0.738
Error	4.504	12	0.375			

Table 4-27 showed the pair wise comparison by treatment for the third week. The mean response of sleepiness for the Active group (2.529) was lower than the mean for the placebo (3.054). A Bonferroni test confirmed that the Active group was significantly less sleepy than the Placebo for the third week of treatment ($p < 0.01$).

Table 4- 27: ***Bonferroni-Pairwise Comparison between treatments groups Week 3***

(I) Treatment group	Mean	Mean Difference (I-J)	Std. Error	Sig.[a]	95% Confidence Interval for Difference[a]	
					Lower Bound	Upper Bound
Active	2.526	.528*	0.091	0.000	0.330	0.725
Placebo	3.054					

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Figure 4-5 shows the pattern of the sleepiness by hour for the third week of assessment. The ability to fall asleep by the respondents is evident between the two groups. For example, the active group showed fewer tendencies to fall asleep when compared against the placebo.

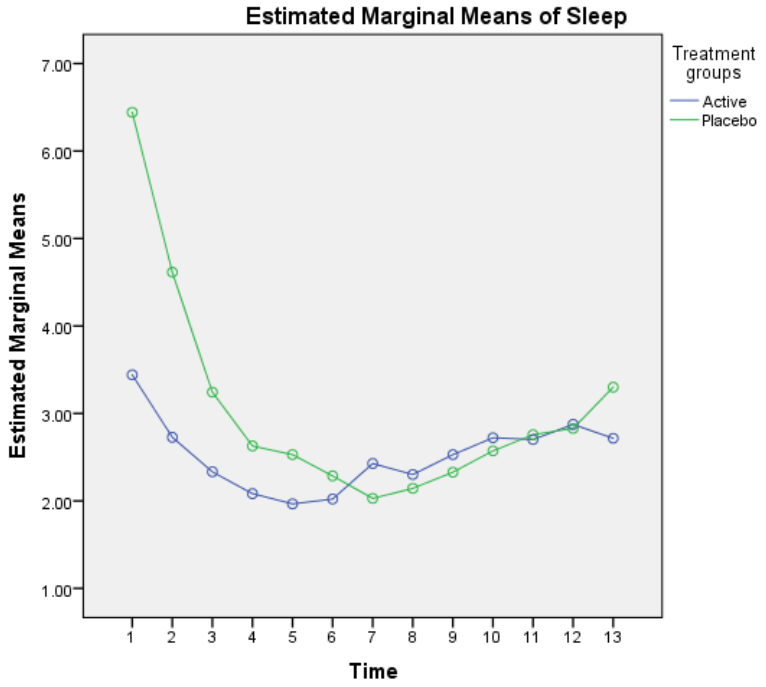


Figure 4- 5: ***Differences in the mean scores estimate at week 3***

4.5.5 Mauchly's Test of Sphericity by Weeks

Table 4-28 showed the test for sphericity for the participants rating of their sleepiness. The Mauchly test has a p-value of 0.005, which suggests evidence of heterogeneity of covariance of the responses. The greenhouse-Geisser adjustment of the ANOVA (F) test was therefore used in assessing the sleepiness on the SSS by weeks.

*Table 4- 28**: Mauchly's test of Sphericity by Weeks***

Mauchly's Test of Sphericity[a]

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	Df	Sig.	Epsilon[b]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
Time	0.632	10.553	2	0.005	0.731	0.799	0.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. Design: Intercept + Group

Within Subjects Design: Time

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

4.5.5.1 Descriptive Statistics

Table 4-29 illustrate the mean score of the treatment groups by weeks. It can be gathered from the table below that week1 had the highest grading concerning the chances of falling asleep during the day for both the Active and Placebo – this is to be expected as this was the pre-treatment (baseline) period. This tendency was, however, at the lowest for the third week. In addition, it can be observed that the Active treatment showed an improved tendency to reduce sleepiness throughout the period of assessment when compared against the Placebo.

*Table 4- 29**: Descriptive statistics***

Treatment groups		Mean	Std. Deviation	N
	Active	3.5293	0.88934	13
Week1	Placebo	3.5901	0.96808	13
	Total	3.5597	0.91129	26
	Active	3.0904	0.62346	13
Week2	Placebo	3.6077	0.9874	13
	Total	3.3491	0.85095	26
	Active	2.5263	0.40487	13
Week3	Placebo	3.0539	1.21937	13
	Total	2.7901	0.92992	26

4.5.5.2 ANOVA tests of within-subjects and between effects

As shown in Table 4-30, the mean sleepiness scores for the Active and Placebo group by weeks differed significantly beyond the 0.001 level: F (1.462,35.089) = 27.610; p< 0.001 (with Greenhouse-Geisser adjustment). This suggests that the tendency to fall asleep was different for the Active and Placebo group by weeks of observation. Partial eta squared = 0.535 representing a large effect. There was also significant interaction between groups and time: F (1.462, 35.089) = 3.101; p < 0.001 (with Greenhouse-Geisser adjustment). Partial eta squared =0.114 representing a large effect.

*Table 4- 30**: Tests of Within-Subjects Effects by Weeks***

Source		Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Time	Greenhouse-Geisser	8.227	1.462	5.627	27.610	0.000	0.535
Time * Group	Greenhouse-Geisser	0.924	1.462	0.632	3.101	0.000	0.114
Error(Time)	Greenhouse-Geisser	7.151	35.089	0.204			

As shown in Table 4-31, the mean scores for the treatment groups of the participants rating of the SSS failed to show any significant differences beyond 0.05 level: F (1, 24) = 1.277; p > 0.05. Partial eta squared = 0.051 representing a medium effect.

*Table 4- 31**: Test of Between-Subjects Effects by Weeks***

Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	815.25	1	815.25	393.21	0	0.942
Group	2.649	1	2.649	1.277	0.27	0.051
Error	49.76	24	2.073			

Table 4-32 lists the Bonferroni comparisons of the respondent sleepiness assessed by weeks with Active and Placebo treatment. The tendency to fall asleep for week One were not significantly higher than for Week Two (P>0.05). Week three scores differed

significantly from week one and week two, which suggest that both groups experienced reduction in chances of falling asleep at the end of the study. (P<.0001).

*Table 4- 32**: Bonferroni-Pairwise Comparison between groups by Weeks***

(I) Weeks		Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
					Lower Bound	Upper Bound
1	2	0.211	0.098	0.126	-0.042	0.463
	3	.770*	0.135	0.000	0.423	1.117
2	1	-0.211	0.098	0.126	-0.463	0.042
	3	.559*	0.081	0.000	0.35	0.768
3	1	-.770*	0.135	0.000	-1.117	-0.423
	2	-.559*	0.081	0.000	-0.768	-0.35

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Figure 4-6 further illustrates the difference of the mean ability to fall asleep of the participants treated with both Active and Placebo. The difference is evident for the three weeks. For the Active group, for example, it can be observed that there was a consistent reduction in the tendency to fall asleep from week one to week three. In contrast, the first and second weeks for the Placebo group exhibited the same tendency to fall asleep. Significant improvement was only observed at the third week of treatment.

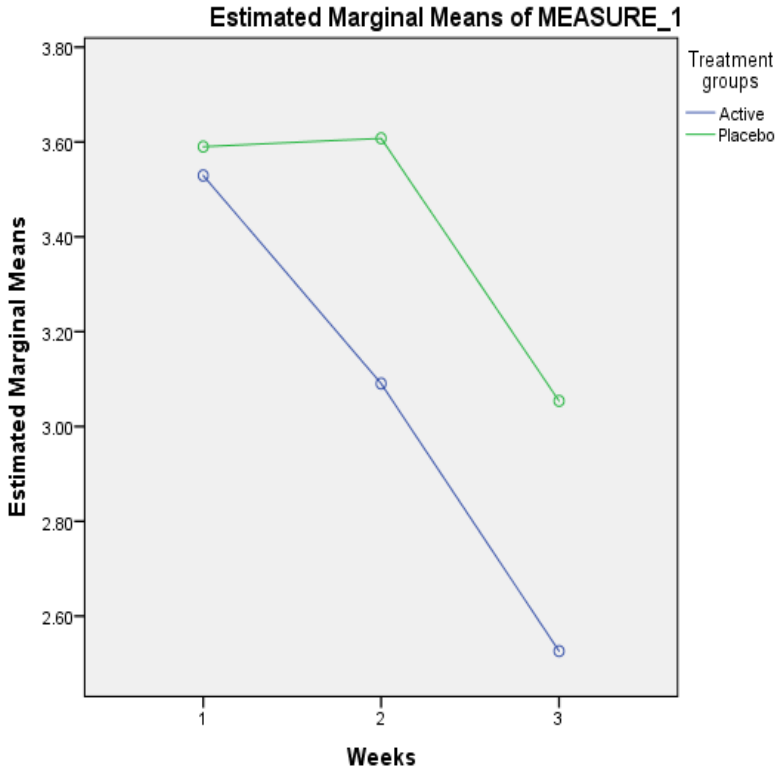


*Figure 4- 6****: Differences by weeks in the sleepiness of respondents***

4.6 Conclusion

Both group experienced statistically significant decreases in ESS scores according to intra-group analysis of ESS data i.e. all participants were less sleepy at the end of the study; intergroup analyses however did not reveal any significant differences between groups. Overall, however the mean ESS values measured in the Herbal complex group were consistently lower than the Placebo group and when calculating sleep sufficiency, the Herbal complex group appeared to have responded more favourably than those receiving placebo.

Furthermore, and with regards to the SSS data, it was gathered that the tendency to fall asleep in the morning (7am) remain unchanged throughout the weeks of assessment. Notwithstanding this, the Active group showed significant improvement in the participant's sleepiness after the commencement of treatment (week two and three). In contrast, improvement was only noticeable for the Placebo group at week three. Overall, the Active group showed fewer tendencies to fall asleep than the Placebo group for week two and three, which suggests that the degree of sleepiness was effectively managed with the Active treatment. Conclusively, this chapter showed that the ESS and SSS score were highly reliable in assessing the degree of sleepiness during the day.

CHAPTER 5

5.1 Introduction

The present study examined the efficacy of a herbal complex (*Rhodiola rosea, Gingko biloba, Panax ginseng & Bacopa monerii)* in management of excessive daytime sleepiness. This chapter focuses on discussing the results that were well presented in the previous chapter.

Participants were tertiary education students of Durban University of Technology (DUT) (Durban) located in KwaZulu-Natal, students were targeted in this study because they are a sector of the population recognized to be significantly affected by excessive daytime sleepiness as it was reported that 70.6% of students have less than 8 hours of sleep per night and often stay awake all night (Hershner and Chervin, 2014). The prevalence of EDS amongst students is well documented in a number of studies; in Brazilian medical students 39, 5% (Rodrigues *et al*, 2002), 35% in Peru (Whittier *et al*, 2013), 28% in Chile (Concepcion, 2013), 26 % in Ethopia (Robinson *et al*, 2013) and 27% in Taiwan University (Tran *et al*, 2013).

5.2 Sample demographics

The age range of the participants in this study was set at 18-30 years as per inclusion criteria, the American National Sleep Foundation reported 59% of adults between the ages of 18-29 years described themselves as being night owls. This study comprised 67,7% males (21 of 31) and 32,3% females (10 of 31) which suggested that the male gender amongst DUT students was more affected by EDS – however this should be interpreted with caution since non-probability convenience sampling was applied and the research sample was small. Despite this, these findings do concur with existing literature; the incidence amongst medical students in the Southern part of South India reported that males (52,06%) were more commonly affected by EDS than females (47,10%) (Ramamoorthy *et.al*, 2014). Similarly, a study at University of Hawaii also recruited more males (29) than females (13) (Ramilo, 2015) and the prevalence of EDS was 4,5% in Korean males and 3,2% in Korean females (Kim *et al*, 2004).

One can thus conclude that despite the small sample size and the sampling method applied in this study the gender distribution is congruent with that of existing research.

With respect to age distribution, the placebo group had a slightly higher mean (23±3.46) than the active group (22± 2.71). However, the result did not significantly differ based on age and gender and the was no significant difference in ages in both groups (See Table 4.3). This is expected since the inclusion criterion had a limited age range of 18-30.

Participants were randomly divided into two groups, Group one was the active group that consisted of 67.7 % (21 of 31) of the participants and group two was the placebo group that had 32.3% (10 of 31) of participants. All prospective participants had to have a total ESS score of 10 or more to be considered for inclusion as previous studies indicated that any score of less than 10 was considered as normal sleep (Mahoney et al, 2014) and a score of greater than 10 suggested EDS (Baldwin *et al*, 2004) (Banerjee, 2007). For week 1 of the SSS the Bonferoni test (table 4-19) failed to show significance in the respondents ability to fall asleep ($p > 0.05$) i.e. the groups were statistically similar at baseline in terms of their SSS scores, similarily baseline ESS scores were also not statistically dissimilar, confirming a similar degree of sleepiness between the groups at baseline.

Although this study did not collect formal data surrounding the impact of EDS on student life most of the participants reported poor concentration, overwhelming need to sleep, unintended falling asleep and feeling of drowsiness as their signs and symptoms (especially after lunch) (Morrison *et al*. 2012) in the beginning of the study. Feeling tired or sleepy especially during the day is something that most perceived as normal: Many had learned to live with EDS because they think it's part of who they are. Some of the participants mentioned that during certain times of the day they had to rest ("sleep") to rejuvenate their mind and gain more energy to carry them through the rest of the day. Others blamed their ESS on the afternoon lectures, when the sun is too hot, after a heavy meal, attending a boring lecture, lecture rooms being crowded and others had poor sleeping patterns (they do not have enough sleep and depend on different energy drinks to sustain them during the day).

5.3 Discussion of ESS data

The ESS Cronbach's alpha for the active group was 0.564 which suggested that the was no consistency but the placebo group Cronbach's alpha was 0.896 and across the whole sample the combined Cronbach's alpha was 0.777 indicative of internal consistency (See Table 4.4). John (1992) also reported high levels of consistency between the 8 situations accessed in the ESS as measured by Cronbach's alpha (0.74-0.88).

The Fisher's exact test compared individual variables of the ESS (8 settings) between groups at the three intervals of measurement and showed no statistically significant differences between the active and placebo group in all variables and all intervals and none had a p-value of < 0.05 (See Table 4.5). However, at the end of the study there were some improvements noted in both active and placebo groups as demonstrated by Table 4.5 (ESS participants rating), although not significant ESS scores were consistently lower in the active group.

Intra-group analyses of ESS data clearly confirm significant improvement in ESS scores in response to placebo and active treatment i.e. both groups had significantly lower ESS scores post intervention, this improvement is also clearly noticeable when reviewing the decrease in mean ESS scores over time.

Despite the presence of obvious reductions in mean ESS scores the inter-group ANOVA tests revealed no statistically significant differences between groups that none of the p-value was significant (See Table 4.13). Despite this, the mean values of the active group were lower than the placebo group at close out (See Table 4.14).

The ESS is reported to be the most discriminating test of daytime sleepiness; it clearly showed the impact of the drug Modafinil in reducing the EDS in narcoleptics (Johns, 2000) and in another study a high ESS score of patients suffering from OSA returned to normal after successful treatment (Ramilo, 2015). The trend observed in this study of reduction in mean ESS scores in response to treatment is arguably supportive of existing literature indicating this tools ability to reflect changes in EDS in response to treatment this is clearly observable when comparing ESS_1/2 readings with ESS_3.

5.4 Discussion of SSS data

The SSS readings were found to be reliable in determining whether the herbal complex was effective in reducing EDS or not. As it was seen in the previous chapter, where the chances of sleepiness were assessed hourly, 7AM was found to be the time of day when participants were sleepiest, this suggests that the participants woke up unrefreshed and tired, and picked up during the day especially between 10 AM to 1PM through the course of the study. Bonferroni tests revealed that the active group was significantly less sleepy than the placebo group hourly (tables 4-23 & 4-27) and this was confirmed by the mean scores in figure 4-4 & 4-5).

A basic comparison of SSS means clearly reveals a significant reduction over time within the active group (Table 4-29) In the beginning of the study (week 1) the active group had a mean score of 3.5293 that decreased to 2.5263 (i.e. 28% reduction) at the end of the study (week 3) while the placebo group had 3.5901 at baseline that reduced to 3.0539 (i.e. 14.9% reduction). It is interesting to note that although both group's week 3 scores were significantly less than their respective weeks 1 and 2 ($p<0.0001$), in the active group the decrease in SSS score occurred consistently and was already statistically less by week 2 where as in the placebo group significant improvement was only observed at the third week of treatment (see Figure 4.6).

Although the mean pre-treatment (baseline) score for sleepiness for Active group (3.529) was slightly lower than the Placebo (3.590), a Bonferroni test (table 4-19) failed to show significance in the respondents ability to fall asleep ($p> 0.05$) i.e. the groups were statistically similar at recruitment. When comparing respective groups at the end of week 2 the data revealed that there was a statistically significant difference between the groups (see table 4.21 and 4.22) and the Bonferroni test confirmed that the Active group was significantly less sleepy than the placebo group (see table 4.23). Similar findings were seen when the groups were compared at the end of week 3, (see table 4.25, 4.26, 4.27) i.e. the Active group was significantly less sleepy than the placebo group.

Overall, the SSS was statistically effective and was able to prove that the herbal complex was more effective than the placebo and it also able to show consistent improvement throughout the weeks, as it seen in another study where it was found to be useful in measuring sleepiness in patients with narcolepsy in response to

treatment (Shahid et.al., 2010) and reduction of daytime sleepiness in patients with a history of mild snoring (Scharf et.al, 1994).

5.5 Conclusion

In conclusion in terms of the ESS both groups improved significantly over time; degrees of improvement however were not statistically dissimilar although a review of mean scores indicates the active group as having lower scores suggesting a clinically significant trend.

SSS data however confirmed statistically significant differences between groups in favour of the active group confirming the herbal complex superior effect over placebo in the treatment of EDS.

CHAPTER 6

This chapter will conclude the findings of this study and then present recommendations for the future studies.

6.1 Introduction

The aim of the study was to determine the efficacy of the herbal complex (Ginkgo biloba, Panax ginseng, Bacopa monerri & Rhodiola rosea) in the management of excessive daytime sleepiness in terms of the ESS and SSS.

6.2 Study findings

In terms of ESS data, statistically the improvements seen in both groups did not differ from each other significantly, i.e. both groups improved however a clinically significant trend was observed in the active group which had lower ESS mean scores.

In terms of the SSS data, it was revealed that there were notable changes between the two groups, however the herbal complex was more effective than the placebo and it was also able to show consistent improvement throughout the weeks.

The hypothesis that the respective herbal complex would have a beneficial effect in the management of excessive daytime sleepiness in term of the ESS and SSS was statistically proven.

The overall results were pleasing and supported the herbal complex in the management of excessive daytime sleepiness when it was statistically tested in terms of the ESS and SSS.

6.3 Benefits of the study

A significant number of participants did experience an improvement in their presented signs and symptoms that were associated with excessive daytime sleepiness.

Others gained information about Homoeopathy, since the majority did not know about the profession.

Participants were educated about their health, especially regarding their eating and sleeping habits and they were also advised not to rely on energy drinks or any caffeinated drinks further they were advised that they should have at least 6 hours of sleep.

6.4 Limitation of the study

- The sample size of this study was small (n=31) largely due to budgetary limitations and the scope of a coursework mini-dissertation
- The study was limited to tertiary students within KwaZulu-Natal
- The study was limited to participants between the age of 18-30 years
- The study was limited to participants with no any other medical conditions

6.5 Recommendations

The following recommendations are made for further research:

1. It would be advisable to increase the sample size of the study to ensure more reliable statistical data – based on anecdotal reports from participants and the rapid rate at which suitable participants were recruited and existing literature on prevalence of EDS amongst students the researcher is of the opinion that the population suffering from EDS is relatively large and accessible a larger study of this nature is thus feasible.
2. The duration of the current study was limited (3 weeks) this was due to a number of factors including but not limited to; budget constraints and time constraints – although a clinically significant tread of improvement was noted

a study of longer duration may highlight a greater distinction between the placebo effect and therapeutic benefit.

3. Future research should consider other options of control such as sleep hygiene.
4. Conduct a comparative study, comparing a homoeopathic complex to a homoeopathic simillimum and a herbal complex in management of excessive daytime sleepiness.
5. Future studies should stratify the sample for gender to ensure an equal distribution amongst males and females.
6. Future studies that recruit students should consider the timing of recruitment and treatment to avoid exam periods.
7. Future studies of this nature should consider qualitative measures and/or a patient reported outcome measure.
8. Conduct the same study using the same herbs but administered separately to see the most effective herb.
9. So to avoid risking the double blinding status of the study, future trials should consider a double dummy design.

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APPENDICES

APPENDIX A: RESEARCH ADVERTISMENT

Sleepy during the day?

Are you a DUT student suffering from Excessive Daytime Sleepiness?

Research on this topic is being conducted at the DUT Homeopathic Day Clinic as part of three M.Tech: Homoeopathy studies.

If you are interested in participating and to see if you qualify please contact:

Ntombizethu Mbatha 081 8348 155

Sindisiwe Mazibuko 079 2244 698

Nondumiso Shabangu 076 1129 187

The homoeopathic clinic 031 373 2041

APPENDIX B: LETTER OF INFORMATION AND CONSENT FORM

LETTER OF INFORMATION

Title of the Research Study: The efficacy of a herbal complex in management of excessive daytime sleepiness

Principal Investigator/s/researcher :(Name, qualifications)
Sindisiwe Sthembile Mazibuko- Bachelor's degree in technology: Homoeopathy

Co-Investigator/s/supervisor/s:(Name, qualifications)
Dr David Naude – Master's Degree in Technology: Homoeopathy

Thank you for showing interest in this study.

Brief Introduction and Purpose of the Study:
The reason for this study is to test a herbal medicine on a common problem called Excessive Daytime Sleepiness (EDS). EDS is a condition where you feel sleepy or tired during the daytime when you should be alert.

Outline of the Procedures:
If you voluntarily respond to one of our advertisements on campus we will call you back and with your permission ask you a series of short questions to see if you are a suitable participant for the research, this should take less than 5 minutes, we will also answer any questions you may have regarding the study – we are only including 30 participants in this study and once we have obtained 30 we will not take in any further participants.

You qualify to participate in this study if you must:

- Be between 18 and 30 years of age
- Be a registered tertiary education student
- Be willing to follow the respective research process including 3 consultations with the researcher as well as comply with the research protocol and provide written informed consent (give us your permission in writing confirming you want to participate)
- Be in a general good state of health
- Have a ESS score of greater or equal to 10 [which suggests excessive sleepiness] – this is a questionnaire we will complete with you when we see you.

We cannot include you if you:

- Are younger than 18 or older than 30

- Are currently taking chronic or acute medication (orthodox, homoeopathic, herbal or other) for any medical condition
- Use any recreational drugs and drugs of abuse
- Suffer or have a history of narcolepsy, obstructive sleep disorder (apnoea), mood disorders or circadian rhythm disorders (we will check this for you when we see you)
- Are currently suffering from any chronic or debilitating disease
- Are a night shift workers or have travelled internationally within the last 6 weeks
- Are commercial/occupational drivers, machine operators or pilots or have a history of sleep-associated incidents.

If you meet these criteria and want to participate we will book you an appointment at the Homoeopathic Day Clinic at DUT where you will meet us for the first consultation. The first consultation will take about 60 minutes to complete, we will ask you to provide written consent (permission) to participate after we have explained everything to you and given you time to ask any questions you may have.

Once this is done we will take detailed medical history (set of questions about your health history) and then do a basic physical examination which similar to what you would have done with your general practitioner. We will then fill in a questionnaire (ESS questionnaire) with you which tells us how sleepy you get during the day. After this you will be sent home with another questionnaire called a SSS which you will complete daily for 1 week, this also measures generally how alert you are during the day. One week later you will come back to the clinic and meet us again for 15 minutes only; at this point you will hand in the SSS which you have filled in and we will give you the medicine that we would like to test.

For the next two weeks you will take this medicine and continue filling in the SSS questionnaire on a daily basis. After two weeks of taking the medicine you will come back to the clinic for a 3rd time to meet us for 30 minutes where you will hand in the SSS questionnaires you filled in and we will fill in another ESS questionnaire. We will also do a final check and examination before you finish the study.

The medicine we are testing is a herbal medicine (natural medicine) which is used regularly in homoeopathic clinics, it is considered to be safe and there should be no side effects or dangers from taking this medicine, you will have to take the medicine for two weeks and we will supply you with enough medicine for this time. It is also important to note that 1/3 of participants i.e. 10 out of 30 will not get an active medicine, they will get a placebo (inactive medicine) this is necessary for use to test how well the active medicine works and is commonly done in medical research. You will only be told if you got the active medicine or the placebo at the end of the study but if you were on the placebo we will offer you one free consultation and bottle of medicine at the end of the study.

Process	**How long**	**What will happen and where**
Telephone call (we will call you back)	5 minutes	With your permission we will ask you a set of questions to see if you qualify for the study over the phone
1st consultation	60 minutes	At the homoeopathic day clinic on Ritson Campus Case history (questions) Basic physical examination ESS questionnaire
2nd consultation (1 week later)	15 minutes	At the homoeopathic day clinic on Ritson Campus Hand in questionnaire Receive medicine

		Receive instructions
3rd consultation (2 weeks later)	30 minutes	At the homoeopathic day clinic on Ritson Campus Hand in questionnaires Case history (questions) Basic physical examination Referral if needed

Risks or Discomforts to the Participant:
Participating should not result in you experiencing any discomfort or any significant risks; we do not need to perform any painful procedures in this research.

Benefits:
If you receive the active medicine you may feel less sleepy and more alert during the daytime, if you were on the inactive placebo you will get 1course of free treatment for this at the end of the study for your daytime sleepiness. The researcher is doing this research to obtain her Master's degree in Homoeopathy from DUT.

Reason/s why the Participant May Be Withdrawn from the Study:
At any time during the study you can choose to withdraw/stop the study without having to provide a reason for leaving; further if you leave there will be no negative consequences for you. We may stop you participating in the study if you don't following the instructions given or if you don't come for your appointments or if we feel you no longer meet the requirements for the study – if we do so we will refer you to the necessary doctor for further treatment if you need it.

Remuneration:
There will not be any payment for your participation in this study.

Costs of the Study:
Participating in the study will not cost you anything, i.e. you will not have to pay for the consultations or the medicines you receive while on this study.

Confidentiality:
We will protect your identity and personal information; your file will be safely locked away and will not be available to anyone except the researcher and her supervisor. When we write up the research we will not mention any names and everything you tell us in the consultations is confidential as it would be in any doctor's visit.

Research-related Injury:
It is highly unlikely that you will sustain any harm or injury from participating, however if you were to get sick or develop an allergy we will refer you to the necessary doctor who can take care of you.

Persons to Contact in the Event of Any Problems or Queries:

Research supervisor: Dr David Naude 0317652514 or 0823701012
Researcher: Sindisiwe Sthembile Mazibuko 0792244698
Institutional Research Ethics administrator on 031 373 2900.
Complaints can be reported to the DVC: TIP, Prof F. Otieno on 031 373 2382 or dvctip@dut.ac.za.

APPENDIX B: LETTER OF INFORMATION AND CONSENT FORM

CONSENT

Statement of Agreement to Participate in the Research Study:

- I hereby confirm that I have been informed by the researcher, _____ (name of researcher), about the nature, conduct, benefits and risks of this study - Research Ethics Clearance Number: _____,
- I have also received, read and understood the above written information (Participant Letter of Information) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

_____ _____ _____ _____

Full Name of Participant **Date** **Time** **Signature / Right Thumbprint**

I, _____ (name of researcher) herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____ _____

Full Name of Researcher **Date** **Signature**

_____ _____ _____

Full Name of Witness (If applicable) **Date** **Signature**

_____ _____ _____

Full Name of Legal Guardian (If applicable) Date **Signature**

APPENDIX C: STANFPRD SLEEPINESS SCALE

Stanford Sleepiness Scale

"Alertness Test"

The Stanford Sleepiness Scale is a quick and easy way to assess how alert you are feeling.
Discover your own pattern of alertness by recording your "degree of sleepiness" at different times throughout the day.

Using the 7-point scale below pick what best represents how you are feeling and note the corresponding number on the chart below.

Degree of Sleepiness	Scale Rating
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not fully alert	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; losing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7
Asleep	X

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
7am							
8am							
9am							
10am							

11am							
12pm							
1pm							
2pm							
3pm							
4pm							
5pm							
6pm							
7pm							
8pm							
9pm							
10pm							
11pm							
12am							

What does this all mean?

Ideally, you would like a score of "1" for each of the hours you are awake. A result of 4 or below may indicate that you could be suffering from a lack of sleep. Getting a better nights rest could improve your level of alertness and day to day performance.

Use this tool to help schedule your classes during times you are most alert!

APPENDIX D: EPWORTH SLEEPINESSCALE

The Epworth Sleepiness Scale

0 = would **NEVER** doze
1 = **SLIGHT** chance of dozing
2 = **MODERATE** chance of dozing
3 = **HIGH** chance of dozing

SITUATION	CHANCE OF DOZING (0-3)
Sitting and reading	
Watching television	
Sitting inactive in a public place (e.g. a theater or meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	
TOTAL SCORE	

SCORE RESULTS:

1-6 Congratulations, you are getting enough sleep!

7-8 Your score is average

9+ Very sleepy and should continue to seek sleep assistance.

APPENDIX E: CASE TAKING FORM

Note:

- For any symptom: description now, **location, sensation, aetiology, modalities, concomitants, history, treatment/ management** so far.
- If no symptoms for any section of the case, write **NAD (No Appreciable Disease)** in the space provided.

1. **MAIN COMPLAINT/S**:

APPENDIX E: CASE TAKING FORM

2. **PAST MEDICAL HISTORY:** Childhood illnesses, vaccinations, hospitalization, surgery. Accidents. Any other chronic illnesses still currently active e.g. hypertension, diabetes, asthma.

Allergies:_____

If the patient does not understand the question, **do not pursue** it because you will not get useful information.

Smoking History: TYPE/BRAND_____

- Number of cigarettes per day_____÷ 20 = A
- Number of years _____= B
- Number of pack years_____ = A x B

A pack year is a measure of exposure/ risk. Equivalent to smoking a 20-cigarette pack a day for one year. Work this out after taking the case if need be.

Alcohol History: TYPE OF DRING_____

- Everyday? YES/ NO
- Average number of drinks: cans/bottles/cartons beer_____
  : Bottle wine_____
  : Bottles spirits_____

---

3. **CURRENT MEDICINES**: Pharmaceutical or other, including **contraceptive pill/injection**, **HRT, sleeping tablets.**

Name:	For:

Current Supplements: (Vitamins, special drinks etc)

Name:	For:

4. **FAMILY MEDICAL HISTORY**:

MOTHER	FATHER

MOTHER'S MOTHER	FATHER'S MOTHER
MOTHER'S FATHER	FATHER'S FATHER
SIBLINGS	

---

5. **GASTROINTESTINAL**: Indigestion, heartburn, cramps, flatulence, appetite, cravings and aversions. Aggravations. Thirst.

TYPE OF DRINK:	QUANTITY PER DAY:
How many teaspoons of sugar in tea/ coffee?	How many cups a day?

6. **BOWEL FUNCTION**: Constipation, diarrhea, hemorrhoids (**detail is necessary only if problem is present**).

APPENDIX E: CASE TAKING FORM

7. **URINATION**: Frequency, urgency, pain. (**detail is necessary only if UTI is present**). **Males over 40 years of age: strength of stream, stop-start, pain on ejaculation = Prostate.**

8. **MENSTRUATION**: Duration of overall cycle and regularity, duration of menses, volume, colour, consistency, pain, concomitants (e.g. headaches, constipation, diarrhea etc). **Menarche**. **Pre-menstrual symptoms**. Date of start of last menstrual period. **Pregnancies** – how many [reason for termination], complications, including post-natal depression. **Peri-menopause**: all of the above, as well as symptoms of hot flushes, dry skin, dyspareunia, mood swings. **Menopause**: age of onset. Brief history of menstruation i.e. any problems with menstruation?

9. **GENITALS**: Eruptions, discharge, infections. Females: history of thrush.

10. **SEXUALLY ACTIVITY**: Any problems? Desire/libido? History of **STD's. HIV STATUS**? **Cd4 Count** if positive. When? **How many partners**? **Emotions regarding a positive status? Education regarding safe sex.**

11. **CHEST**: Problems with breast, breathing, cardiac.

12. **HEAD**: Ears, eyes, nose, throat/ voice. Headache: **painkillers**? Name, how many, how often? **Issue of medication overuse headache** (= **rebound headache** due to **addiction/dependency**. **Combination ingredient medicines worse than single ingredient medicines**. **Medication overuse** is defined in terms of **treatment days per month**, such that **treatment occurs at least three months**. The headache is present **on more than 15 days per month**.

13. **SLEEP:** Pattern, quality, position. Dreams (only worth pursuing if outstanding/ recurrent dreams)

14. **SKIN**: Current and history, rashes, warts, boils, pimples, easy bruising, rate of healing.

15. **MUSCULOSKELETAL**: Location, modalities, concomitants (e.g. weather changes).

16. **GENERAL**: Energy, weather preferences.

17. **MENTAL**: Ask things that have not already come up in the consultation. **Do not go over that material again unless it seems appropriate to do so**. If you had to **describe yourself**, what **type of person** would you say you are? / What are you **characteristics**? / What is your **personality**? Anxiety / worries, anger, sadness/ depression. **Relationships**. **What makes you happy**?

APPENDIX F: SOAPE NOTES AND TREATMENT RECORD

PATIENT DETAILS

DATE: / / 2015	**Patient's name & surname:**

S

MAIN COMPLAINT(S)

1.	**3.**
2.	**4.**

ON EXAMINATION

BP: / mmHg	**OBSERVATION (Unusual)**
PULSE: bpm	
RESP: bpm	
Temp:	
WEIGHT: kg	
URINE DIPSTICK:	**PREGNANCY:**

GENERAL EXAMINATION

Jaundice	
Anaemia	
Cyanosis	
Clubbing	
Oedema	
Dehydration	
Lymphadenopathy	

SYSTEM REVIEW

Respiratory Examination	
Cardiovascular Examination	
Abdominal Examination	
Musculoskeletal Examination	

A

DIAGNOSIS (MEDICAL)

ICD-10 CODE:	**Written Diagnosis:**

CENTRE OF THE CASE

1.	**3.**
2.	**4.**

CASE ANALYSIS

MENTALS	GENERALS	PARTICULARS

RUBRICS [3]

P

REMEDY DIFFERENTIALS

1.	**4.**
2.	**5.**
3.	**6.**

PRESCRIPTION

1.	**2.**	**3.**	**4.**
Rx:	**Rx:**	**Rx:**	**Rx:**
Mitte:	**Mitte:**	**Mitte:**	**Mitte:**
Sig:	**Sig:**	**Sig:**	**Sig:**

E

PATIENT EDUCATION/ADVICE

1.
2.
3.

SIGNATURES

Clinician's Name:	**Student's Name: Sindisiwe Mazibuko**	**Dispenser's name:**
Clinician's Signature:	**Student's Signature**	**Dispenser's Signature:**
Date:	**Date:**	**Date:**

APPENDIX G: APPLICATION FOR RECRUITING DUT STUDENTS

Ms Sindisiwe Mazibuko
E8004 Section 5
Madadeni, 2951
Cell: 0792244698

8 February 2016

Professor S. Moyo
Director of Research - DUT

Re: Permission to recruit DUT students for M.Tech: Homoeopathy research

I *Sindisiwe Mazibuko* currently registered for M.Tech qualification at Durban University of Technology: Homoeopathy department am kindly requesting permission to advertise and recruit DUT students to participate in my M.Tech: Homoeopathy research. This will be done by placing approved research posters on various notice boards as well as by word of mouth.

Research topic
The efficacy of a herbal complex (*Rhodiola rosea, Gingko Biloba, Panax Ginseng, Bacopa monerii)* in the management of excessive daytime sleepiness

Purpose of the study
To determine the efficacy of a *herbal complex* (*Rhodiola rosea, Gingko Biloba, Panax Ginseng, Bacopa monerii)* in the treatment of Excessive Daytime Sleepiness using the Epworth Sleeping Scale and Stanford Sleeping Scale.

Methodology
I will be required to consult with 30 patients obtained by convenience sampling, each having three consultations at the DUT Homoeopathic Day Clinic over a period of three weeks each, Clinical supervision will be provided by my Supervisor (Dr D. Naude) or a consenting Clinician on Duty. The study is considered to be of 'minimum risk' to participants and approval has been sought from the Faculty of Health Sciences Research and Higher Degrees Committee and the IREC respectively.

Yours sincerely
Sindisiwe Mazibuko

APPENDIX H: PERMISSION TO CONDUCT RESEARCH AT DUT

Directorate for Research and Postgraduate Support
Durban University of Technology
Tromso Annexe, Steve Biko Campus
P.O. Box 1334, Durban 4000
Tel.: 031-3732576/7
Fax: 031-3732946 E-mail: moyos@dut.ac.za

7th October 2016

Ms Sindisiwe Mazibuko c/o
Department of Homoeopathy Faculty
of Health Sciences
Durban University of Technology

Dear Ms Mazibuko

PERMISSION TO CONDUCT RESEARCH AT THE DUT

Your email correspondence in respect of the above refers. I am pleased to inform you that the Institutional Research Committee (IRC) has granted full permission for you to conduct your research "The efficacy of a herbal complex *(Rhodiola rosea, Ginko Biloba, Panax Ginseng, Bacopa Monerii)* in the management of excessive daytime sleepiness" at the Durban University of Technology.

We would be grateful if a summary of your key research findings can be submitted to the IRC on completion of your studies.

Kindest regards.
Yours sincerely

[redacted]

_____

PROF. S. MOYO

APPENDIX I: APPLICATION FOR USING HOMOEOPATHIC DAY CLINIC

Ms Sindisiwe Mazibuko
E8004 Section 5
Madadeni, 2951
Cell: 0792244698

8 February 2016

Dear Drs
C. Hall (HOD)
C. Korporaal Clinic Director
S. Nienaber Clinic Co-ordinator

Re: Permission to use the Homoeopathic day clinic

I *Sindisiwe Mazibuko* currently registered for M.Tech qualification at Durban University of Technology: Homoeopathy department am kindly requesting gatekeeper permission to use the Homoeopathic Day Clinic (HDC) for consulting with my research patients for the purpose for my research, as I am required to complete my partial dissertation by the end of 2016.

Research topic

The efficacy of a herbal complex (*Rhodiola rosea, Gingko Biloba, Panax Ginseng, Bacopa monerii)* in the management of excessive daytime sleepiness

Purpose of the study

To determine the efficacy of a *herbal complex* in the treatment of Excessive Daytime Sleepiness using the Epworth Sleeping Scale and Stanford Sleeping Scale.

Methodology
I will be required to consult with 30 patients, each having three consultations at the HDC over a period of three weeks each. Clinical supervision will be provided by my Supervisor (Dr D. Naude) or a consenting Clinician on Duty, and I agree to follow all rules and policies relating to the HDC.

Yours sincerely
Sindisiwe Mazibuko

APPENDIX J: PERMISSION TO USE HOMOEOPATHIC CLINIC

MEMORANDUM

To : Prof Ross
Chair : RHDC

Prof Adam
Chair : IREC

From : Dr Charmaine Korporaal
Clinic Director : FOHS Clinic

Date : 19.09.2016

Re : Request for permission to use the Homoeopathic Day Clinic for research purposes

---

Permission is hereby granted to:

Ms Sindisiwe Mazibuko (student number 21110208),

Research title:"The efficacy of a herbal complex (*Rhodiola rosea, Gingko Biloba, Panax Ginseng, Bacopa monerii)* in the management of excessive daytime sleepiness".

It is requested that Ms Mazibuko submit a copy of her RHDC / IREC approved proposal to the Clinic Co-ordinator (Dr Nienaber) before she starts with her research in order that any special procedures with regards to her research can be implemented prior to the commencement of data capture.

Thank you for your time.

Kind regards

[redacted]

Dr Charmaine Korporaal

Clinic Director : FOHS Clinic

Cc: Dr Nienaber : Clinic Co-ordinator
Dr D Naude : Supervisor
Mrs Linda Twiggs : Student Clinic Co-ordinator

APPENDIX K: ETHICAL CLEARANCE

Institutional Research Ethics Committee
Faculty of Health Sciences
Room MS 49, Mansfield School Site
Gate 8, Ritson Campus
Durban University Of Technology

P O Box 1334, Durban, South Africa, 4001

Tel: 031 373 2900
Fax: 031 373 2407

I I October 2016
IREC Reference Number: REC 72116

Ms S S Mazibuko
E8004
Section 5 Madadeni
2951

Dear Ms Mazibuko

The efficacy of a herbal complex (Rhodiola rosea, Gingko Biloba, Panax Ginseng, Bacopa monerii) in the management of excessive daytime sleepiness

The Institutional Research Ethics Committee acknowledges receipt of your gatekeeper permission letter.

Please note that FULL APPROVAL is granted to your research proposal. You may proceed with data collection.

Yours Sincerely,

[redacted]

Professor J K Adam

Chairperson: IREC

APPENDIX L: RANDOMISATION LIST

MAZIBUKO RANDOMISATION LIST		
Prover Name and Number (Fill in the patient's name in the order they were recruited into the study)	Dispense the respective medication according to the column in which the lies,	
	Active	Placebo
1	√	
2		√
3	√	
4	√	
5		√
6	√	
7		√
8	√	
9		√
10	√	
11	√	
12		√

13	√	
14	√	
15	√	

MAZIBUKO RANDOMISATION LIST		
Prover Name and Number (Fill in the patient's name in the order they were recruited into the study)	Dispense the respective medication according to the column in which the lies,	
	Active	Placebo
16		√
17	√	
18	√	
19	√	
20		√
21		√
22	√	
23	√	
24		√
25	√	
26	√	

27	√	
28	√	
29	√	
30		√

Patient Name and Number (Fill in the patient's name in the order they were recruited into the study)	Dispense the respective medication according to the column in which the lies.	
31	√	
32	√	
33		√
34	√	
35		√